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TUMOR ANTIBODY PRODUCTION/ CHARACTERIZATION/ DETECTION

1. A NOVEL HUMAN T CELL ANTIGEN PREFERENTIALLY EXPRESSED ON MATURE T CELLS AND SHARED BY BOTH WELL AND POORLY DIFFERENTIATED B CELL LEUKEMIAS AND LYMPHOMAS.

Kamoun M, Kadin ME, Martin PJ, Nettleton J, Hansen JA
Dept. Lab. Medicine, Univ. Washington SB-10, Seattle, WA, 98195
J Immunol; 127(3):987-991 1981

A new lymphocyte differentiation antigen shared by all normal T cells and some malignant B cells was defined by a monoclonal antibody designated 12.1. This antibody reacted with all peripheral blood T cells but not with normal B cells and B cell lines. Analysis with a fluorescence activated cell sorter showed that the expression of 12.1 antigen changes during T cell maturation. Most thymocytes, blasts of acute T cell leukemia, and cells from established leukemic T cell lines bear a small amount of 12.1 antigen. In contrast the majority of peripheral blood T cells, activated T cells, and leukemic T cells of the Sezary syndrome bear a large amount of 12.1 anti-

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gen. Unexpectedly, antibody 12.1 reacted with leukemic cells from most patients with B-type chronic lymphocytic leukemia (CLL) and some patients with lymphosarcoma cell leukemia (LSCL). Among these leukemias, expression of the 12.1 antigen was not correlated with the stage of B cell maturation, with the amount of surface immunoglobulin on the cells, or with the presence or absence of monoclonal gammopathy. In a comparative serologic analysis the antigen defined by antibody 12.1 was distinct from the p67 T cell antigen (defined by monoclonal antibody 10.2) that is also known to be expressed by B-type CLL cells. (Author abstract) (22 Refs)

2. DISTRIBUTION OF HLA CLASS 1 ANTIGENS IN NORMAL HUMAN TISSUE AND IN MAMMARY CANCER.

Fleming KA, McMichael A, Morton JA, Woods J, McGee JO'D

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J Clin Pathol; 34(7):779-784 1981

With a monoclonal antibody which reacts with all HLA Class 1 antigens it was found that these antigens are not uniformly distributed in all nucleated cells. Rather HLA Class 1 antigens are restricted in their distribution to lymphoid cells, endothelial cells of small vessels, and certain epithelia including mammary duct cells. These antigens were not detected on hepatocytes, specialized cells of the central nervous system, or on the tumor cells of 8 out of 17 human mammary cancers. Given the hypothesis that T cells only respond to foreign antigens on cells which share a common major histocompatibility antigen, these results imply that the T cell responses to viral infections of hepatocytes - for example, hepatitis B virus and the CNS - for example, subacute sclerosing encephalitis, are mediated through an antigen system other than HLA Class 1. The absence of HLA Class 1 antigen on many mammary cancer cells may be of prognostic significance if T cell modulation of tumor growth is mediated through this class of antigens. (Author abstract) (19 Refs)

3. IMMUNOPOTENTIATING ACTIVITY OF WHOLE CELLS AND MINI-CELLS OF SALMONELLA TYPHIMURIUM.

Kurashige S, Yoshida T, Kodama K, Mitsuhashi S

College Medical Care and Technology, Gunma Univ., Showa-machi, Maebashi, Gunma 371, Japan

Microbiol Immunol; 25(5):467-477 1981

The effect of whole cells of an avirulent strain of Salmonella typhimurium and its mini-cells on humoral immunity, cellular immunity and phagocytosis of macrophages was studied in Balb/c, ICR, and DBA/2 mice. The iv inoculation with both whole cells and mini-cells produced stimulation of phagocytosis of mouse peritoneal macrophages; mini-cells were 1,000x less effective than whole cells. Both whole cells and mini-cells enhanced cell-mediated immunity against leukemia L1210 and sarcoma 180 cells. Whole cells stimulated the antibody-forming cells to produce IgG antibody of higher affinity. Mini-cells stimulated slightly blast cell transformation of lymphocytes from mesenteric lymph nodes of normal mice. (19 Refs)

4. AN IMMUNOCYTOCHEMICAL STUDY OF NON-HODGKIN'S LYMPHOMAS.

Pangalis GA, Nathwani BN, Rappaport H

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Cancer; 48(4):915-922 1981

Lymph node specimens obtained intraoperatively and/or at autopsy from 89 patients with non-Hodgkin's lymphoma were studied immunohistochemically. The peroxidase anti-peroxidase (PAP) technique was used for detecting monoclonal cytoplasmic immunoglobulin (CIg) and for determining the classes and types of immunoglobulins in the tumors. Following rigid criteria, monoclonal CIg was demonstrated in 4 (16%) of 25 cases of nodular, poorly differentiated lymphocytic lymphoma (NPDL); in 3 (14%) of 21 cases of diffuse, poorly differentiated lymphocytic lymphoma (DPDL); and in 13 (30%) of 43 cases of diffuse histiocytic lymphoma (DH). Of the four NPDL patients, two had the Mkappa, one the Akappa, and one the lambda chain type. Of the three DPDL patients, one had the Mkappa, one the Gkappa, and one the lambda chain type. Of the 13 DH patients, 5 had the Mkappa, 4 the Akappa, 1 the GMkappa, 1 the Alambda, 1 the Glambda, and 1 the kappa chain type. In two DH patients negative for cytoplasmic immunoglobulins, cytoplasmic lysozyme was present, indicating the histiomonocytic nature of the tumor cells. There was no significant difference between the overall survival rates for the DH patients with or without monoclonal CIg. In all three types of lymphoma studied, we encountered many patients (67%) who had tumor cell populations without demonstrable CIg and few patients (11%) with polyclonal CIg. There are several possible reasons why many of the patients were PAP-negative and why some had polyclonal cell populations. The PAP method may be useful in establishing the monoclonal nature of neoplastic lymphoid cell populations. (Author abstract) (49 Refs)

5. COMPLEMENT FIXATION BY IGM AND IGG AUTOANTIBODIES ON CULTURED HUMAN GLIAL CELLS.

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J Neurosurg; 55(1):19-26 1981

The humoral immune response to autologous gliomas has been investigated in 16 patients using immune adherence and anti-C3 immunofluorescence assays of serum samples. Significant antiglioma antibody activity was detected in 56% of these sera. Fractionation experiments demonstrated that IgM class antibodies were more effective than IgG in their ability to fix complement on cultured glioma cell membranes. In addition, autologous IgG was shown to inhibit IgM complement-fixing activity in some experiments. 'Capping' of immune complexes on the glioma cell surface is also described. (Author abstract) (26 Refs)

6. UBIQUITOUS CELL-SURFACE GLYCOPROTEIN ON TUMOR CELLS IS PROLIFERATION-ASSOCIATED RECEPTOR FOR TRANSFERRIN.

Sutherland R, Delia D, Schneider C, Newman R, Kemshead J, Greaves M

Membrane Immunology Lab., Imperial Cancer Research Fund, Lincoln's Inn Fields, London WC2A 3PX, England

Proc Natl Acad Sci USA; 78(7,part2):4515-4519 1981

A murine monoclonal antibody (OKT9) raised against human leukemic cells binds to a wide variety of leukemia and tumor cell lines and to a minority of leukemia cells taken directly from patients. Fetal thymus and liver are strongly reactive as are some normal, immature hemopoietic cells and activated lymphocytes. Reactivity with OKT9 appears to correlate with proliferation status in both normal and malignant populations. Biochemical analysis indicates that this structure is a approx 180,000-dalton glycoprotein with two disulfide-bonded subunits of approx 90,000-daltons. Isolation of the transferrin receptor from a T-cell line (MOLT-4) indicates that it also has a dimeric approx 180,000-dalton structure. Radio-labeled transferrin bound to its receptors can be specifically precipitated by the monoclonal OKT9, although the latter does not bind transferrin itself, indicating that the antigenic structure defined by this antibody is likely to be the transferrin receptor. (Author abstract) (37 Refs)

7. THE G-IX ANTIGEN OF MURINE LEUKEMIA VIRUS: AN ANALYSIS WITH MONOCLONAL ANTIBODIES.

Pierotti M, DeLeo AB, Pinter A, O'Donnell PV, Hammerling U, Fleissner E

Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY

Virology; 112(2):450-460 1981

The GIX antigen of murine retrovirus gp70 is a marker for virus replication in various cell types, as well as for T-cell differentiation and leukemogenesis in particular mouse strains. The serological definition of GIX depends on the cytotoxicity of a particular rat antiserum for thymocytes from strain 129 mice. We have found that two rat monoclonal antibodies, elicited by immunization with AKR ecotropic virus or AKR leukemia cells, co-type closely with GIX in several assay systems. Like GIX, the epitopes identified by the monoclonal antibodies are amplified on thymocytes during leukemogenisis in AKR mice. These antibodies are cytotoxic for GIX+ leukemia cells and for fibroblasts infected with GIX+ viral serotypes. Though absorbed by GIX+ thymocytes of various strains, the antibodies are not cytotoxic for these cells. We ascribe the latter result to lower representation of antigenic sites on normal thymocytes, and postulate that more than one epitope may participate in classical GIX-mediated cytotoxicity. The monoclonal antibodies do not react with viral env products synthesized in the presence of the inhibitor of glycosylation, tunicamycin. Reactivity with the antibodies appears to require a stable configurational change in the env precursor protein coinciding with glycosylation, rather than direct participation of carbohydrate in the antigenic site. Thus subsequent enzymatic removal of carbohydrate chains in vitro does not alter reactivity with the antibodies. (Author abstract) (42 Refs)

8. A MONOCLONAL ANTIBODY AGAINST A BURKITT LYMPHOMA ASSOCIATED ANTIGEN (MEETING ABSTRACT).

Wiels J, Fellous M, Tursz T

No affiliation given

Immunobiol; 159(1/2):31 1981

A monoclonal antibody, referred to as 38.13, was obtained by fusing murine myeloma cells with Lewis rat splenocytes sensitized with Daudi cells (human Burkitt lymphoma, containing Epstein-Barr virus genome, but lacking HLA A, B, C and beta2 microglobulin molecules at the cell surface). 38.13 antibody was demonstrated to be a rat IgM. By complement-dependent microcytotoxicity and indirect immunofluorescence assays, 38.13 antibody was shown to react specifically with cells derived from Burkitt tumors, including both Epstein-Barr virus genome carrying and Epstein-Barr virus negative Burkitt lymphoma. By contrast Epstein-Barr virus containing lymphoblastoid cell lines, derived from normal B lymphocytes, were not recognized by 38.13 antibody. Malignant fresh cells from patients affected with various lymphoproliferative disorders were negative, except 4/8 cases of abdominal Burkitt-like lymphomas. Normal lymphocytes from peripheral blood, spleen, lymph node, tonsil and bone-marrow and mitogen (phytohemagglutinin, pokeweed mitogen and Concanavalin A) activated blasts were also negative. Thus 38.13 antibody apparently recognized a Burkitt-associated antigen, which is clearly not related to Epstein-Barr virus. The pattern of reactivity of 38.13 antibody with various Burkitt lymphoma cells appeared quite heterogenous, and some Burkitt were constantly negative. 38.13 antibody could thus define a peculiar subgroup of Burkitt lymphoma. (no Refs)

9. SELECTIVE DETECTION OF TUMOR MHC ANTIGENS BY IGG2 AND NOT IGG1 ALLOANTIBODIES (MEETING ABSTRACT).

Tartakovsky B, De Baetselier P, Feldman M, Segal S

Department of Cell Biology, The Weizmann Institute of Science, Rehovot, Israel

Immunobiol; 159(1/2):194 1981

In view of the determining role of the major histocompatibility complex (MHC) in controlling and restricting the function of killer T-lymphocytes against modified self components, one could expect that the modulation of MHC-encoded antigens on malignant cells may create different communications with the host's immune system. It was, therefore, of interest to analyze whether H-2 alloantigens expressed on malignant tissues would be recognized differentially by anti H-2 antibodies, as compared with H-2 antigens expressed on normal somatic cells. We report here, observations indicating that tumor associated MHC antigens select preferentially anti H-2 antibodies belonging to the IgG2 isotype, while normal somatic cells bind comparable amounts of anti H-2 antibodies of both IgG1 and IgG2 subclasses. In this study, we have used anti H-2 antisera raised against fetal tissues. Those antisera were found to contain high titers of both IgG1 and IgG2 antibodies. The tumors analyzed were 1) the Lewis Lung Carcinoma (3LL), 2) a methylcholanthrene induced fibrosarcoma (T-10), 3) an ascitic lymphoma (EL-4). (no Refs)

10. PRODUCTION OF MONOCLONAL ANTIBODIES REACTIVE WITH THE NEOPLASTIC LYMPHOCYTES OF CUTANEOUS T CELL LYMPHOMA (MEETING ABSTRACT).

Berger C, Takezaki S, DePietro W, Chu A, Morrison S, Edelson R
Departments of Dermatology and Microbiology, Columbia University, New York, NY
J Invest Dermatol; 76(4):311 1981

To obtain monoclonal antibodies reactive with cutaneous T cell lymphoma (CTCL) lymphocytes, splenic B cells from immunized BalbC mice were hybridized with a Balb C myeloma line. Four thousand hybridoma clones were screened for reactivity with CTCL cells using an affinity purified I126-rabbit anti-mouse reagent in a radioimmunoassay (RIA). Fifty reactive hybridoma clones producing monoclonal anti-human lymphocyte antibodies were isolated. Monoclonal antibody specificity was determined by RIA and indirect immunofluorescence using a cytofluorimeter. Two monoclonal antibodies (BE1 and BE2) were of particular interest since they were reactive with antigens on the surface of CTCL cells, but absent from the surface of normal peripheral blood mononuclear cells. BE1 and 2 were reactive with an Epstein-Barr virus transformed B cell line. These antibodies recognize relatively minor immunogens on the CTCL cell surface since they were produced by only 2 of the 50 clones. BE1 was present on neoplastic T cells from each of 6 CTCL patients and immunoprecipitated a molecule that under reducing conditions had 2 chains with mol wt of 27,200 and 25,800 daltons. BE2 was present of 3 of 6 CTCL patients and a MOLT 3 T cell line. These results indicate that CTCL cells express membrane antigens present on cells from certain transformed cell lines but not on normal blood mononuclear cells. Monoclonal antibodies against these membrane antigens should provide valuable diagnostic and research tools. (no Refs)

11. HUMAN MONOCLONAL ANTIBODIES TO TUMOR CELL SURFACES (MEETING ABSTRACT).

Sikora K
MCR Clinical Oncology Unit, Cambridge CB22QQ, England
Clin Sci; 60(3):3P 1981

Several groups have investigated the production of monoclonal antibodies to a variety of tumors. Although such xenogenic antibodies are of considerable interest, it is the antigenic determinants seen as foreign by the patient's immune system that we most wish to identify. These determinants are more likely to provide the necessary specificity for diagnostic monitoring and therapeutic exploitation. Lymphocytes obtained from hilar and bronchial lymph nodes from 23 patients undergoing radical surgery for carcinoma of the bronchus were fused in polyethylene glycol with either a mouse myeloma (NS 1) or a rat myeloma (Y3). Hybrids were selected by growth in a tissue culture medium that inhibited the growth of the parent myeloma. 62% of the resultant hybrids were found to be secreting human immunoglobulin as detected by a sensitive protein A sheep RBC assay. Immunoglobulins synthesized by such hybrids were internally labelled with tritiated thymidine and their binding activity to a variety of membrane preparations was determined. Nine monoclonal antibodies were found which bound to molecules present on lung cancer membranes and not on normal lung membranes from the same patient. Immunoglobulin production by the hybrid cells ceased by the tenth wk after fusion, presumably due to loss of the relevant chromosome. Additional antitumor antibodies have been prepared by the fusion of intra-tumoral lymphocytes from a patient with a poorly differentiated glioma. No binding to normal brain membranes was observed. (no Refs)

12. MONOCLONAL ANTIBODIES REACTIVE WITH HUMAN MAMMARY TUMOR CELLS (MEETING ABSTRACT).

Colcher D, Horan Hand P, Nuti M, Austin F, Schlom J
National Cancer Institute, Bethesda, MD, 20205
4th Annual San Antonio Breast Cancer Symposium, Nov 6-7, 1981, San Antonio, Texas Cancer Therapy and Research Center of South Texas; 1981

Splenic lymphocytes of mice immunized with membrane-enriched fractions of metastatic human mammary carcinoma tissues were fused with the NS-1 non-immunoglobulin (Ig) secreting murine myeloma cell line. This fusion resulted in the generation of hybridoma cultures secreting Igs reactive in solid phase radioimmunoassays with extracts of metastatic mammary carcinoma cells from involved livers, but not to extracts of apparently normal human liver. After further screening of immunoglobulin reactivities and double cloning of cultures, eleven monoclonal antibodies were chosen which demonstrated reactivities with human mammary tumor cells. These monoclonals have been placed into at least five major groups based on their differential binding to the surface of various live human mammary tumor cells in culture, to extracts of mammary tumor tisues, and to tissue sections of mammary tumor cells employing the immunoperoxidase technique. One of the monoclonals was highly reactive in antibody-dependent cell mediated cytotoxicity assays on a variety of human mammary tumor cells in culture. Whereas a spectrum of reactivities to mammary tumors was observed with the eleven monoclonals, no reactivity was observed to apparently normal cells of the following human tissues: breast, lymph node, lung, skin, testis, kidney, thymus, bone marrow, uterus, thyroid, intestine, liver, bladder, tonsils, stomach, and prostate. None of the monoclonals showed binding to purified ferritin or carcinoembryonic antigen. Monoclonal antibodies of all five major groups, however, demonstrated binding to human metastatic mammary carcinoma cells both in axillary lymph nodes and at distal sites. (no Refs)

13. DEVELOPMENT OF A SPECIFIC AND SENSITIVE ASSAY FOR THE DETECTION OF ANTIGENS IN COMPLEX MIXTURES AND ITS APPLICATION TO THE DELINEATION OF AN AUTOCHTHONOUS HUMORAL ANTI-TUMOR RESPONSE.

Cantarero LA
The University of Iowa, Iowa City, IA
Diss Abstr Int (B); 42(1):68-B 1981

A solid-phase immunoassay (the a-ELISA) was chosen as the assay system. Representation of all tumor-associated proteins (TAAs) on the solid-phase absorber was obtained by studying the adsorptive characteristics of radiolabeled proteins and protein mixtures for polystyrene (the solid-phase material used in this investigation) and determining conditions under which stable non-competitive binding of each protein present in these mixtures occurred. Subisotypes of rat IgG as well as corresponding monospecific antiimmunoglobulin reagents were prepared. Using these and similarly prepared reagents, the ability of the a-ELISA to discriminate among antibodies of different classes and subclasses was demonstrated. Approx one nanogram of specific antibody of any isotype could be detected. This assay system was used to study the autochthonous humoral anti-tumor-host interactions in a radiation-induced adenocarcinoma of the rat small intestine. The distribution of TAAs by mol wt as well as the distribution of antibodies of different classes and subclasses were investigated. In all tumor animals studied, tumor-associated antigens were found in at least two broad peaks in sucrose density gradients corresponding to proteins of 70,000-140,000 and 300,000-600,000 mol wt. Immune responses to these TAAs were restricted to IgM and IgG2a, the latter usually in the form of immune complexes, especially in the serum of older tumor-bearing rats. The response seemed more pronounced against the faster-sedimenting TAAs (heavier mol wt) and was never greater than a few ug of antibody per ml of serum. The data collected on the IgG2a anti-tumor antibody were consistent with the conclusion that it was a covalent dimeric immunoglobulin molecule. (no Refs)

14. RECOVERY OF ANTIBODY PRODUCTION IN HUMAN ALLOGENEIC MARROW GRAFT RECIPIENTS: INFLUENCE OF TIME POSTTRANSPLANTATION, THE PRESENCE OR ABSENCE OF CHRONIC GRAFT-VERSUS-HOST DISEASE, AND ANTITHYMOCYTE GLOBULIN TREATMENT.

Witherspoon RP, Storb R, Ochs HD, Flournoy N, Kopecky KJ, Sullivan KM, Deeg HJ, Sosa R, Noel DR, Atkinson K, Thomas ED
Div. Oncology, Fred Hutchinson Cancer Res. Center, 1124 Columbia St., Seattle, W A, 98104
Blood; 58(2):360-368 1981

One-hundred fifty-three recipients of HLA-identical sibling marrow transplants for aplastic anemia or hematologic malignancy were injected with bacteriophage phiX174 (phage), pneumococcal polysaccharide antigen (PPA), or keyhole limpet hemocyanin (KLH). Antibody levels were determined several times in the 6 wk after injection. Multiple regression techniques were used to determine what factors played significant roles in the antibody response. The most significant factors were the time elapsed from transplantation, chronic graft-versus-host disease (GVHD), and antithymocyte globulin (ATG) treatment. All patients had low antibody responses to all antigens in the first 180 days from transplant. Beyond 180 days patients without chronic GVHD showed antibody responses indistinguishable from those of normal donors. However, patients with chronic GVHD had the following impairments: (1) primary response to phage, (2) conversion from IgM to IgG in secondary response to phage, (3) secondary response to KLH, and (4) response to PPA. ATG treatment given to patients either prophylactically or therapeutically for acute GVHD was followed by lower primary responses to phage in the first 180 days and poor ability to switch from IgM to IgG antibody in the secondary response beyond 180 days postgrafting. Other factors did not yield additional significant information about ability to predict antibody responses including diagnosis, conditioning regimen, treatment in or out of laminar air flow rooms, transplantation in remission or relapse of hematologic malignancy, pretransplant refractoriness of the recipient to platelet transfusions from random donors, donor age or donor sex, and steroid administration for treatment or prevention of GVHD. The data indicate that, given enough time after transplantation, the ability to reproduce normal antibody function recovers except in those patients experiencing chronic GVHD. (Author abstract) (32 Refs)

15. PURIFICATION AND CHARACTERIZATION OF L-DOPA DECARBOXYLASE, A MARKER FOR HUMAN TUMORS WITH NEUROENDOCRINE DIFFERENTIATION (MEETING ABSTRACT).

Maneckjee R, Francis J, Baylin SB
The Johns Hopkins Medical Institutions, Baltimore, MD, 21205
63rd Annual Meeting of the Endocrine Society, June 17-19, 1981, Cincinnati, Ohio. The Endocrine Society 385 pp., 1981.

In this work, human dopa decarboxylase (DDC) has been purified for the first time to near homogeneity from human pheochromocytoma. The enzyme preparation migrates as a single protein with correlating enzyme activity on polyacrylamide gel electrophoresis. It has a mol wt of 112,000 as measured by gel filtration. Similar mol wt were obtained for DDCs from human kidney, small cell carcinoma (SCC) and neuroblastoma. Electrophoresis under denaturing conditions reveal the enzyme to be a multi-subunit protein. The isoelectric point for pheochromocytoma DDC is pH 4.5. Human DDC appears to be a nonglycosylated protein based upon failure to bind various lectins and it requires pyridoxal phosphate and free sulfhydryl groups for max activity. It decarboxylates L-dopa abd 5-hydroxytryptophan, but is practically inactive towards tryptophan, tyrosine and phenylalanine. The Km for L-dopa was found to be 1.7x10(-4) at pH 7.2. Antibodies were elicited against the purified enzyme. The specificity of the antiserum was demonstrated by immunoelectrophoretic and immunodiffusion analysis, as well as by specific second antibody precipitation of DDC activity. Quantitative antibody binding studies revealed cross-reactivity between DDC from human pheochromocytoma, neuroblastoma, ganglioneuroma, medullary thyroid carcinoma (MTC), SCC and kidney and between human DDC and that from rat MTC, adrenals and liver. The specific antibody to DDC may serve as a useful tool to determine the cells responsible for endocrine differentiation in multiple tissues. (no Refs)

16. AN IMMUNORADIOMETRIC ASSAY FOR ESTROGEN RECEPTOR IN BREAST CANCER (MEETING ABSTRACT).

Greene GL, Jensen EV

The Ben May Laboratory for Cancer Research, The University of Chicago, Chicago, IL, 60637

63rd Annual Meeting of the Endocrine Society, June 17-19, 1981, Cincinnati, Ohio. The Endocrine Society 385 pp., 1981.

We report here the development of an assay for human estrophilin that uses two monoclonal rat antibodies (D547Spgamma and D75P3gamma, both IgG) that bind to different regions of the receptor molecule. Simultaneous binding of these antibodies to the 4S [3H] estradiol-receptor complex (ER) has been shown by the formation of a ternary immune complex (Ab1 ER Ab2) that sediments more rapidly (11-13S) in salt-containing sucrose density gradients than complexes formed between ER and either antibody alone (Ab ER, 8-9S). Neither antibody interacts with progesterone or androgen receptors of MCF-7 human breast cancer cells. When polystyrene beads coated with D547Spgamma IgG are incubated overnight at 4 C or for 2 hr at 23 C with MCF-7 cytosol E R in phosphate-buffered saline containing normal rat serum, the binding of ER to the beads is directly proportional to the amount of added ER over a range of at least 5-1000 fmol of ER. The amount of ER bound to the antibody-coated beads has been determined by direct measurement of [3H] estradiol on the beads after incubation with ER, and by measuring the amount of 125I-labeled D75P3gamma IgG bound after a second incubation with labeled antibody for 2 hr at 23 C. Beads coated with monoclonal B72Spgamma IgG, an antibody specific for calf uterine ER, were used as negative controls. When tumors cytosols from ten human breast cancers were assayed for estrophilin content by this immunoradiometric method in the absence of estradiol and the results were compared with ER content determined by the sucrose density gradient method, the relative rankings of receptor levels by both methods was the same for all ten tumors over a range of 0-3000 fmol of ER per gram of tissue. (no Refs)

TUMOR ANTIBODIES ASSOCIATED WITH VIRUSES

17. THE SPECIFIC INTERACTION OF THE ROUS SARCOMA VIRUS TRANSFORMING PROTEIN, PP60SRC, WITH TWO CELLULAR PROTEINS.

Brugge JS, Erikson E, Erikson RL
Dept. Microbiology, Sch. Medicine, State Univ. New York, Stony Brook, Long Island, NY, 11794
Cell; 25(2):363-372 1981

Sera from rabbits bearing tumors induced by Rous sarcoma virus (RSV) were previously found to contain antibody to the RSV transforming protein, pp60src. Two additional transformation-specific phosphoproteins from RSV-transformed avian cells are immunoprecipitated with these sera. These proteins, having mol wt of 90,000 (pp90) and 50,000 (pp50), are not precipitated from uninfected or transformation-defective virus-infected cells and are not related to any RSV structural proteins. Normal uninfected chicken cells contain a protein that shares identical partial proteolytic cleavage peptides with the pp90 protein immunoprecipitated from RSV-transformed cells. This pp90 protein is one of the major cytoplasmic proteins in uninfected cells. Antibody directed against pp90 also immunoprecipitates pp60src and pp50 from lysates of RSV-transformed chicken cells. (Author abstract) (33 Refs)

18. CELL-MEDIATED AND HUMORAL ANTIBODY RESPONSES TO VIRALLY INDUCED TUMOURS.

Walia AS, Lamon EW
Dept. Surgery, Univ. Alabama, Birmingham, AL, 35294
Indian J Med Res; 73:410-419 1981

Thymus-dependent cell-mediated immunity is strongly implicated in resistance to virus induced tumors by the fact that neonatal thymectomy increases the incidence of tumor development even in genetically resistant strains of mice. Evidence is presented in this report that the humoral and cell-mediated arms of the immune response can cooperate at the effector level for the destruction of virus-induced tumor cells. Specific humoral antibodies can cause lymphocytes to be cytotoxic against polyoma and M-MuSV induced tumor cells in vitro. Studies of the mechanism involved in antibody-dependent cell-mediated cytotoxicity have revealed that the effector cells include thymocytes. Cortisone resistant medullary thymocytes are most reactive and both IgM and IgG antibodies induce specific cell-mediated cytotoxicity. (Author abstract) (37 Refs)

19. GOAT LYMPHOSARCOMA FROM BOVINE LEUKEMIA VIRUS.

Olson C, Kettmann R, Bersey A, Kaja R
Dept. Veterinary Science, Univ. Wisconsin-Madison, 1655 Linden Drive, Madison, WI, 53706
JNCI; 67(3):671-675 1981

A goat given inoculations of sheep lymphocytes from cultures that produced bovine leukemia virus (BLV) died 8 yr later with lymphosarcoma. The tumors were located in various lymph nodes, the mesentery, omentum, body wall, and retrobulbar tissues. The BLV had been cultured from lymphocytes during the 1st yr after the goat's infection, and persisting BLV antibodies could be demonstrated when the animal was 7.5 yr old. BLV provirus was identified by molecular hybridization in the DNA of the goat tumors at the above five locations. The tumors were similar to those found in lymphosarcoma of the adult bovine type (BLV associated). Normal goat liver, normal calf thymus, and calf-type lymphosarcoma (not BLV associated) served as negative controls. Our serologic, histologic, and molecular hybridization studies are evidence that the lymphosarcoma was induced by BLV. (Author abstract) (14 Refs)

20. HERPESVIRUS-INDUCED ANTIGENS IN SQUAMOUS-CELL CARCINOMA IN SITU OF THE VULVA.

Kaufman RH, Dreesman GR, Burek J, Korhonen MO, Matson DO, Melnick JL, Powell KL, Purifoy DJ, Courtney RJ, Adam E
Dept. Obstetrics and Gynecology, Baylor Coll. Medicine, Houston, TX, 77030
N Engl J Med; 305(9):483-488 1981

Tissue and serum specimens from 19 patients (24-79 yr old) with squamous-cell carcinoma (SCC) in situ of the vulva (10 patients), severe dysplasia (1), condyloma acuminatum (4), and controls seen for periodic check-up (4), were evaluated for herpes simplex virus Type 2 (HSV2) DNA-binding proteins. Nine of 10 biopsy specimens from patients with SCC or severe dysplasia reacted strongly when stained with anti-ICPS34/35 (rabbit antiserum to HSV2-infected-cell-specific protein 34/35), and eight also reacted with anti-VP143 (rabbit antiserum to nonstructural HSV2 protein); five also reacted with anti-ICSP11/12 (rabbit antiserum to HSV2-infected-cell-specific protein 11/12). All the positive reactivity observed with anti-ICSP34/35, anti-ICSP11/12 and anti-VP143 was localized in the cytoplasm rather than the nuclei, as has been previously reported in infected cells. Whole-virion structural antigens were not observed, although serological evidence of previous HSV2 infection was found in patients tested for the presence of antibodies. Serum antibodies to HSV2 were noted in nine patients with SCC, including one with mild dysplasia, and two with normal tissue. The parallel rise in the incidences of HSV2 infection and of vulvar SCC in situ and the demonstration of HSV2-specific proteins in this tissue suggest an association of HSV2 infection with this cancer. (17 Refs)

21. CORONAVIRUS-ASSOCIATED ANTIBODIES IN NASOPHARYNGEAL CARCINOMA AND INFECTIOUS MONONUCLEOSIS.

Arnold W, Klein M, Wang JB, Schmidt WAK, Tramplsch HJ
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Arch Otorhinolaryngol (NY); 232(2):165-177 1981

Particles in the cytoplasm of nasopharyngeal carcinoma (NPC) cells were found which resembled coronaviruses. To determine the nature of these particles serum titer determinations were performed in NPC patients, infectious mononucleosis patients, and a control group. Epstein-Barr nuclear antigen (EBNA) test were made on tumor cells from NPC tissues and cells from cultures infected with coronaviruses. For immunological identification of coronaviruses, the human coronavirus strain 229E was cultured on human fetal lung fibroblast MRC-C cells. Comparison of antibody levels showed clearly higher levels of IgG in NPC patients than in controls. IgA was the same in either group. IgM titer was in the low range in NPC patients. Infectious mononucleosis patients showed similar tiers to the NPC patients. The EBNA test was positive in all NPC cells, negative in cell cultures infected with coronavirus. In immunofluorescence tests serum from NPC patients produced intense fluorescence when applied to coronavirus-infected cells. Known high-titer coronavirus sera did not produce a similar result in MRC cells not infected with coronavirus. Evidently coronaviruses are present in the cytoplasm of NPC tumor cells.

A correlation between the RNA coronavirus and the Epstein-Barr virus suggests a possible interaction between them as a factor in NPC. (35 Refs)

22. FELINE LEUKEMIA - UNIQUE AND CROSS-REACTING ANTIGENS ON INDIVIDUAL VIRUS-PRODUCING TUMORS IDENTIFIED BY COMPLEMENT-DEPENDENT ANTIBODY.

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Int J Cancer; 28(2):209-217 1981

Following exposure to feline leukemia virus (FeLV), cats that resist leukemia produce complement dependent antibodies (CDA) which lyse leukemia cells in the presence of cat complement. The CDA activity has been shown to be directed to feline oncornavirus-associated cell membrane antigen (FOCMA) found on the surface of most feline leukemias. Despite the retrovirus etiology of feline leukemia, and the ubiquity of FOCMA expression by individual tumors, we found that CDA activity did not cross-react when five feline leukemia lines were compared (FL74, F422, 3272, 3281, and 79-14940). Profiles for CDA mediated lysis of the leukemia target lines were determined for sera from 149 FeLV exposed cats, and animals were identified whose sera would selectively lyse almost any possible combination of tumors from one to five lines tested. Cross absorption and cold target inhibition studies were performed on selected sera, and a spectrum of different antigens was identified which included both individual determinants and antigens shared by some of the tumor lines. Leukemias FL74 and F422 carried a cross-reactive determinant which was distinct from a second antigen shared by 3272 and 3281; lines F422, 3272 and 3281 each also carried a unique antigen. Leukemia 79-14940 did not cross-react with other target tumor lines. Targets of CDA mediated lysis on leukemia cells may be associated with normal feline cell surface antigens, because CDA titers were sometimes reduced after serum absorption with normal cat spleen cells. The relevance of multiple FOCMA determinants is discussed in terms of tumor escape from immunity. (Author abstract) (30 Refs)

23. CHARACTERIZATION OF THE P21 SRC PROTEIN OF HARVEY SARCOMA VIRUS AND RELATED PROTEINS USING MONOCLONAL ANTIBODIES (MEETING ABSTRACT).

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RNA Tumor Viruses, May 20-24, 1981, Cold Spring Harbor, New York. Cold Spring Harbor Laboratory 294 pp., 1981.

The src gene of the Harvey murine sarcoma virus (HaSV) is one representative of a small family of divergent genes, which also includes the src gene of Kirsten sarcoma virus, and an endogenous sarc gene expressed at high levels in the murine hematopoietic cell line 416B. Each known member of the gene family encodes a polypeptide of approx 21,000 daltons (p21) which is associated with a guanine nucleotide-binding activity. Although the various types of p21 differ in primary structure and in extent of phosphorylation in vivo, each can be precipitated using antisera from some rats bearing syngeneic HaSV-induced tumors. In order to better identify and characterize different forms of p21, we have prepared several monoclonal antibody reagents directed against the p21 of HaSV, and have studied the interaction of these antibodies with other forms of p21. These monoclonal antibodies were identified by three criteria: 1) immunoprecipitation of labeled guanine nucleotide bound to an antigen present in partially purified preparations of HaSV p21; 2) specific immunofluorescent staining of HaSV-transformed cells; and 3) immunoprecipitation of 32P-labeled (autophosphorylated) p21 of HaSV. The binding of each monoclonal antibody to other forms of p21 was assessed initially by immunoprecipitation of antigen from extracts of cells expressing the various p21 src (or endogenous sarc) genes. Some of the antibodies appear to recognize determinants shared by most forms of p21, while others display more restricted specificity. (no Refs)

24. MONCOLONAL ANTI-GP70 ANTIBODIES CAUSE IN VIVO REDUCTION OF FRIEND VIRUS INFECTIOUS CENTERS IN LEUKEMIC SPLEENS (MEETING ABSTRACT).

Chesebro B, Britt WJ
Laboratory of Persistent Viral Diseases, Rocky Moutain Laboratories, Hamilton, MT
RNA Tumor Viruses, May 20-24, 1981, Cold Spring Harbor, New York Cold Spring Harbor Laboratory 294 pp., 1981.

Monoclonal antibodies which treated with gp70, p15 and p15E proteins of Friend virus (FV) were obtained from hybridomas derived from spleen cells of mice recovering from Friend virus-induce d erythroleukemia. Two antibodies appeared to have the Friend-Moloney-Rauscher pattern of specificity. One of these was specific for gp70 and the other for p15. Seven other anti-gp70 antibodies and 1 anti-p15 were restricted in reactivity to Friend and Rauscher viruses, and some Friend-MCF viruses. Two to four days after inoculation of monoclonal antibody, three different IgG2a anti-gp70 antibodies caused a 10-to 1000-fold reduction in the number of spleen cells scoring as F-murine leukemia virus infectious centers without reducing the number of leukemic cells containing cytoplasmic viral antigens. Monoclonal IgG2a or IgG2b anti-p15 and IgM anti-gp70 antibodies did not cause this effect in spite of the fact that these antibodies could lyse FV leukemia cells or FV-infected cells in vitro in the presence of complement. One possible mechanism for the reduction of infectious centers by anti-gp70 antibodies was decreased release of infectious virus from cells as a result of antibody-induced modulation of cell surface gp70 molecules. However, the short time interval between exposure to antibody and observation of decreased infectious centers would appear to make this mechanism less likely. These results appeared to mimic the effect of the Rfv-3 gene seen in (B10.A X A) F1 mice 30-60 days after FV inoculation, where virus release was markedly reduced in spite of continued massive splenomegaly. (no Refs)

25. SEROEPIDEMIOLOGICAL STUDY OF HERPESVIRUS TYPE 2 AND CARCINOMA OF THE CERVIX.

Ohwada N
Dept. Obstetrics and Gynecology, Sch. Medicine, Gunma Univ., Maebashi-shi, Guma Pref. 371, Japan
Kitakanto Igaku; 31(2):87-97 1981

Sera obtained from patients with preinvasive and invasive cervical cancer, and ovarian and corpus cancer as well as from healthy control women were tested for neutralizing antibodies to herpesvirus type 1 (HSV-1) and type 2 (HSV-2) in regard to a possible association between HSV-2 and cervical cancer. Antibody titers to each virus type were determined simultaneously by a microtiter technique. The percentage of women with cervical cancer who had anti-HSV-2 antibody was significantly higher than that of patients with corpus and ovarian cancer and control women; cervical cancer patients 81%, corpus and ovarian cancer patients 26%, and control women 20%. However, the percentage of women having anti-HSV-1 antibody in the study group was comparable to that in the control group; cervical cancer patients 37%, corpus and ovarian cancer patients 39%, and control women 28%. The mean titer of neutralizing activity to HSV-2, as given by log2 of the reciprocal of the final serum dilution that exhibited the neutralizing activity, in the cervical cancer group (2.41 +-1.22) was also significantly higher than that in the corpus and ovarian cancer group (0.87 +-0.89) and in the control women (0.83 +-0.97). This difference was independent of age. It has been noticed that in some patients with cervical cancer, especially in the stage of carcinoma in situ, the neutralizing antibody titers decreased significantly after surgical resection of the cancer tissues. These findings suggest a strong association between HSV-2 infection and the establishment of cervical cancer, although it is not clear whether the virus has a causative role in the development of cervical cancer or not. (36 Refs) (In JPN)

26. PLASMA MEMBRANE ENZYMES IN BALB/C LYMPHOMAS WITH EITHER T OR B CELL PROPERTIES. I. 5'-NUCLEOTIDASE.

Zachowski A, Simonin G, Aubry J, Pommier P, Singh SN, Potter M, Paraf A
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J Receptor Res; 2(1):97-118 1981

Membrane-bound 5'-nucleotidase activity was compared in crude extracts and plasma membrane fractions from murine plasmacytomas and thymomas. Clones of the tumor cells, judged representative of different steps in B and T cell differentiation according to surface antigen markers, were derived, respectively, from Abelson virus transformed lymphomas and IgM, IgA, and IgG producing plasmacytomas, and from thymomas with surface antigen markers characteristic of T suppressor and helper cells and of early T cell differentiation. Membrane fractions were obtained through cell lysis and purification. 5'-Nucleotidase activity was characterized by the following criteria: 1) optimal pH for enzyme activity (7.5-9.5 for B type lymphocytes and 5.5-6.5 for T type cells, except in Lut 13 membranes where it was 9.5); 2) specificity of 5'-AMP as a substrate at optimal pH (for all B cell categories and Lut 13, 5'-AMP was the best substrate; for the remaining T cell types pNPP was preferred); 3) specific inhibition of 5'-nucleotidase by alpha-beta methylene ADP at optimal pH (B type cells exhibited 50% inhibition between 10 and 300 uM, whereas T type membranes required greater than 1 milliM); and 4) inhibition by EDTA at pH optimum (for B derived and Lut 13 membranes, inhibition of 5'-AMP hydrolysis occurred between 0.1 and 5 milliM EDTA, but in T type cells no inhibition was seen). 5'-Nucleotidase was found to be present on Abelson virus transformed lymphomas, plasmacytomas, and LPS stimulated blasts from nu/nu spleen, but on no thymomas except Lut 13. 5'-Nucleotidase could be a key enzyme in the purine metabolism of B cells, but not in T cells. (50 Refs)

27. VACCINATION IN CHILDREN WITH ACUTE LEUKEMIA AND SOLID TUMOR.

Ikeda T, Baba K, Ha K, Tsuda N, Tawa A, Shu K, Yabuuchi H
Dept. Pediatrics, Osaka Univ. Sch. Medicine, Osaka, Japan
Rinsho Ketsueki; 22(3):325-330 1981

Various vaccines (varicella, measles, mumps, rubella, influenza, BCG, Japanese encephalitis, and diphtheria-pertussis-tetanus) were given as immunizations to 52 children with acute leukemia (25) or solid tumors (27). Varicella vaccine was given to 45/52; skin tests with varicella antigens were positive in greater than 90% of the 42 after vaccination. Because the majority of the vaccinated children developed significantly high antibody responses to the various vaccines, vaccination was recommended even for children with malignancy whose immunological function might be weakened by chemo- or radiotherapy. (21 Refs) (In JPN)

28. SERUM EPSTEIN-BARR ANTIBODY LEVELS IN ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN.

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Cesk Pediatr; 36(5):248-253 1981

The serum levels of Epstein-Barr virus capsid antigen antibody were determined by the indirect immunofluorescence test in 21 children (4 boys and 7 girls, 21-140 mo old) before and after the beginning of treatment. The antibody levels were 289.8 (versus 349.5 in the controls) before treatment and 165.3 after treatment (p less than 0.05). The decrease was from 226.3 to 97.5 in the boys (p 0.01), but there was no decrease in the antibody levels in the girls (475.5 before and after treatment, versus 208.6-280.7 in the controls). A direct immunosuppressive effect of the treatment is suggested as one of the possible causes of the decrease in the antibody level. (22 Refs) (In CZE)

29. ISOLATION OF A NEW ACUTE TRANSFORMING VIRUS FROM AN ALV-INDUCED FIBROSARCOMA (MEETING ABSTRACT).

Neel BG, Wang LH, Hanafusa T, Mathey-Prevot B, Hanafusa H, Hayward WS
The Rockefeller University, New York, NY
RNA Tumor Viruses, May 20-24, 1981, Cold Spring Harbor, New York. Cold Spring Harbor Laboratory 294 pp., 1981.

We have isolated a new virus from extracts of a fibrosarcoma induced by the SR-RSV deletion mutant td 107A. Unlike ALV-induced lymphomas which have elevated levels of myc-specific RNA, but which do not release any acute transforming virus, this fibrosarcoma expressed high levels of RNA related to the transforming gene (fps) of Fujinami sarcoma virus (FSV), and released an acute transforming virus. This virus (16L) is subgroup A, causes transformation of fibroblasts in tissue culture, and induces fibrosarcomas with high efficiency in less than 2 wk following injection into newborn chicks. 16L is replication defective, with a 6.7 kilobases (kb) genomic RNA. T-1 oligonucleotide fingerprinting shows that it contains td 107A-derived sequences, including the cap sequence and 3'-derived sequences of td 107A. In addition, it contains oligonucleotides that have previously been shown to be specific for the fps gene in either FSV and/or UR-1 virus. No oligonucleotides unique to the helper viruses of FSV or UR-1 virus were found. Fibroblasts infected with 16L virus produced a gag-fusion protein slightly larger than the transforming protein of FSV. 16L virus has protein kinase activity and phosphorylates both itself and IgG present in tumor bearing rabbit serum. Since the transforming genes of FSV and UR-1 are related to the same cellular gene, c-fps, these results strongly suggest that 16L arose via recombination between td 107A and c-fps. This interpretation has potentially important implications for the mechanism of generation of the acute transforming viruses. (no Refs)

30. ANALYSIS OF THE AVIAN RETROVIRUS REVERSE TRANSCRIPTASE USING MONOCLONAL ANTIBODIES AND MOLECULAR CLONING PROCEDURES (MEETING ABSTRACT).

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Department of Microbiology, University of Minnesota, Minneapolis, MN

RNA Tumor Viruses, May 20-24, 1981, Cold Spring Harbor, New York. Cold Spring Harbor Laboratory 294 pp., 1981.

The structure and function of the avian retrovirus enzyme reverse transcriptase is being examined using monoclonal antibodies and molecular cloning. Monoclonal antibodies have been generated against the reverse transcriptase from avian myeloblastosis virus (AMV). Four of these antibodies will specifically immunoprecipitate reverse transcriptase from AMV and the B-77 strain of Rous sarcoma virus and will inhibit the polymerase activity of the enzyme. Using immunoaffinity chromatographic analysis the enzyme can be purified in a single step to greater than 95% homogeneity. In addition these antibodies are currently being used to determine the enzymatic activity present in specific proteolytic fragments of the enzyme as well as the structure of the forms of the enzyme in infected cells. DNA sequencing analysis has determined the genomic position of the carboxyl end of the gag protein p15 and Bal 31 digestion is being utilized to correctly juxtapose the amino terminal portion of the polymerase gene in relation to an Escherichia coli lac promoter as well as various eukaryotic promotors for cloning into procaryotic and eukaryotic cells, respectively. (no Refs)

31. MUTANTS OF ROUS SARCOMA VIRUS WHICH AFFECT TRANSFORMED CELL MORPHOLOGY AND EXHIBIT ALTERED PP60SRC MOLECULES (MEETING ABSTRACT).

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RNA Tumor Viruses, May 20-24, 1981, Cold Spring Harbor, New York. Cold Spring Harbor Laboratory 294 pp., 1981.

Four Rous sarcoma virus strain SR-A mutants (ST529, W0101, W0201, W0401), arising from stocks independently mutagenized with one of four different mutagens, cause an elongated, or fusiform (morph f) transformed cell morphology in chicken embryo fibroblasts at 37C. The 'pp60src' species isolated from cells transformed by these mutants possess protein kinase activity, as measured by phosphorylation of IgG heavy chains. However, the mutant 'pp60src' species exhibit an apparent mol wt of 54-55K on sodium dodecyl sulfate (SDS) polyacrylamide gels, in contrast to the 59-60K Mr pp60src species isolated from wt SR-A transformed cells, using the same extraction conditions. This difference was observed both with extraction buffers containing SDS, sodium deoxycholate and NP40, as well as with buffers not containing SDS and sodium deoxycholate. Partial digestion experiments utilizing Staphylococcus aureus V8 protease indicate that all four mutant 54-55K src species are lacking peptides present in the N-terminal half region of wt pp60src molecules. These results suggest that a common, or similar, structural defect in the mutant 54-55K src species is intimately related to, and perhaps the cause of, the morph f phenotype exhibited by cells transformed by these particular mutants. (1 Ref)

32. IMMUNOLOGIC DISSECTION OF THE ANTIGENIC SPECIFICITY INDUCED BY ROUS SARCOMA VIRUS BY MEANS OF MONOCLONAL ANTIBODIES (MEETING ABSTRACT).

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Tumori; 67(2,SupplA):167 1981

Rous sarcoma virus (RSV)-transformed mammalian fibroblasts express a membrane antigen (VCSA) controlled by transforming gene src, the viral genome segment directly responsible for the induction and maintenance of neoplastic transformation. By cloning somatic hybrids of murine myeloma lines with splenic lymphocytes from mice hyperimmunized with RSV-transformed cells, it has been possible to produce a certain number of monoclonal antibodies directed against this antigen. Binding tests between selected monoclonal antibodies and a series of cells from different animal species transformed by RSV have made it possible to show that the VCSA antigen is the result of the combined expression on the cell surface of various antigenic determinants controlled either by host cell genes or viral src genes. It is concluded that the expression of VCSA antigen is not due to the insertion of an individual viral protein on the cell surface, but is the result of a change induced by the product of the src gene on one or more components of the plasma membrane coded by cellular genes. (1 Ref) (In ITA)

33. TUMORIGENICITY, ANTIGENICITY AND IMMUNOGENICITY OF THREE MOLONEY LEUKEMIA VIRUS-INDUCED MURINE T CELL LYMPHOMAS.

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Diss Abstr Int (B); 41(11):4062-B 1981

C3HMT1820, C3HMT1892 and C3HMT1893, three in vitro adapted T cell lymphomas that arose in C3H/He mice infected with the Moloney strain of murine leukemia virus, differed in their ability to grow as tumors when injected into adult syngeneic mice. The cells of each of the lymphomas differed not only in their tumorigenic properties but also in their ability to stimulate the in vitro generation of allogeneic cytolytic cells. Likewise, they differed in their expression of H-2 encoded alloantigens and in their ability to suppress the generation of alloreactive cytolytic cells when present as third parties in allogeneic mixed lymphocyte cultures. Unless chemically modified with added haptenic determinants, none of the lymphomas was able to stimulate the generation of syngeneic cytolytic cells in vitro. C3HMT1820 cells, which readily produced tumors when injected into normal syngeneic immunocompetent mice, were both immunosuppressive and poorly immunogenic. C3HMT1892 cells were similar, but probably less immunosuppressive. In contrast, C3HMT1893 cells were neither immunosuppressive nor were they able to stimulate the generation of syngeneic or allogeneic cytolytic cells. This could be attributed to their lack of significant expression of H-2k encoded alloantigen. Nevertheless, C3HMT1893 cells were not tumorigenic in adult mice, suggesting that components of the immune system other than cytolytic T cells may be involved in their failure to produce tumors in adult syngeneic mice. In fact, C3HMT1893 cells were found to be susceptible to lysis by natural killer cells. (no Refs)

ANTITUMOR ACTIVITY AND IMMUNOTHERAPY

34. HETEROGENEITY OF B-CELL LEUKEMIAS DEMONSTRATED BY THE MONOCLONAL ANTIBODY FMC7.

Catovsky D, Cherchi M, Brooks D, Bradley J, Zola H
MRC Leukaemia Unit, Royal Postgraduate Medical Sch., Hammersmith Hosp., Ducane Road, London W12 OHS, England
Blood; 58(2):406-408 1981

A new monoclonal antibody, FMC7, was studied in 68 patients with chronic B-cell leukemia. All 17 cases of prolymphocytic leukemia (B-PLL) and 8/9 of hairy-cell leukemia were positive. In contrast, FMC7 was negative in 32 of 38 chronic lymphocytic leukemias (B-CLL; p less than 0.001) and four cases of B-cell lymphoma. Four of the six positive B-CLL cases were in 'prolymphocytoid' transformation; two of them had bright membrane Ig (SmIg) staining and may represent an intermediate form between B-CLL and B-PLL. Although there was a tendency for the intensity of the immunofluorescence reaction with FMC7 and SmIg to change in parallel, FMC7 did not correlate with any Ig class. In addition, almost all FMC7-negative B-CLL had weak expression of SmIg. FMC7 is different from other monoclonal antibodies raised against B-lineage cells in that it recognizes only some subsets, presumably those at a late stage of maturation. This property confers diagnostic potential to this reagent and may contribute to the better characterization of the B-cell neoplasias. (Author abstract) (14 Refs)

35. LYMPHOID SUBPOPULATIONS OF PERIPHERAL BLOOD AND SPLEEN IN UNTREATED HODGKIN'S DISEASE.

Posner MR, Reinherz EL, Breard J, Nadler LM, Rosenthal DS, Schlossman SF
Sidney Farber Cancer Inst., 44 Binney St., Boston, MA, 02115
Cancer; 48(5):1170-1176 1981

A panel of monoclonal antibodies with well-defined specificities were used as probes to investigate the phenotypes and lineage of circulating lymphoid cells and splenocytes in untreated patients with Hodgkin's disease. A significant relative and absolute reduction in T cells (anti-T3+) was found only in patients with B-symptoms. There was no alteration in the fraction of helper (anti-T4+) or cytotoxic/suppressor (anti-T5+) T cells circulating in peripheral blood when compared to normals, nor was there activation of these cells as measured by the development of surface Ia (anti-I1+). Circulating T cell subsets were not altered 5 to 14 days after splenectomy. Splenic T cells were increased equally in involved and uninvolved spleen when compared with control spleens obtained from accident victims. These findings indicate that abnormal T cell function in Hodgkin's disease may be the result of subtle alterations in T cells or non-T immunoregulatory mechanisms. (Author abstract) (49 Refs)

36. REJECTION OF ALLOGENEIC TUMOR CELLS GROWING IN MOUSE CEREBROSPINAL FLUID: FUNCTIONAL ANALYSIS OF THE INFLAMMATORY PROCESS.

Doherty PC, Zinkernagel RM, Ramshaw IA, Grant CK
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J Neuroimmunol; 1(1):93-99 1981

In C57BL/6 mice (H-2b) inoculated intracerebrally with P815 mastocytoma (H-2d), the tumor cells multiplied rapidly in the cerebrospinal fluid (CSF) for 5 days, then were completely eliminated from the CSF in the next 3 days. On day 8, the CSF contained large numbers of inflammatory cells, which were identified as potent cytotoxic T-lymphocytes, as well as phagocytic and nonphagocytic cells capable of mediating antibody-dependent cell-mediated cytotoxicity (ADCC) against 51Cr-labeled P815 cells. The cytotoxicity of the CSF cells presumably reflected the activities of K cells and cells of the monocyte-macrophage series. The levels of antibody capable of sensitizing the tumor cells to both ADCC and complement-mediated lysis were about 1,000x higher in the serum than in the CSF on day 9. Spleen cells, obtained on day 8, were much less active in the ADCC test than the CSF inflammatory cells obtained at the same time. Sensitive complement-dependent and lymphocyte-dependent cytotoxic assay systems demonstrated no tumor-specific antibody in the CSF of mice that had recently rejected the allogeneic tumor. The process of cell-mediated tumor rejection did not obviously compromise the blood-CSF barrier to immunoglobulins. (18 Refs)

37. A SECOND MESSENGER REQUIRED FOR NERVE GROWTH FACTOR BIOLOGICAL ACTIVITY?

Heumann R, Schwab M, Thoenen H
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Nature (Lond); 292(5826):838-840 1981

The biological activity of mouse nerve growth factor (NGF) and NGF antibodies introduced directly into the cytoplasm of PC12 pheochromocytoma cells was studied by electron microscope autoradiography. The NGF and NGF antibodies were loaded onto guinea pig RBC ghosts that were then fused with the target cells in monolayer cultures. One ghost contained approx 44,000 NGF molecules or a quantity of antibodies sufficient to neutralize 26,000 NGF molecules. The direct introduction of NGF into the cytoplasm did not induce fiber outgrowth, which occurred only when NGF was added to the culture medium. Conversely, the injected NGF antibodies did not interfere with the fiber outgrowth induced by NGF in the culture medium. These results suggested that the biological effects of NGF are mediated by an interaction with specific cell-surface receptors and the generation of a second messenger, rather than by a direct action of intact NGF in the free cytoplasm or nucleus. (21 Refs)

38. ELEVATED SERUM IMMUNOGLOBULIN E IN BRONCHIAL CARCINOMA: ITS RELATION TO THE HISTOLOGY AND PROGNOSIS OF THE CANCER.

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J Allergy Clin Immunol; 67(5):398-406 1981

Total IgE and specific IgE antibodies against six common allergens were measured in the sera of 217 unselected patients with bronchial carcinoma. Their median total IgE level was significantly increased as compared to the median levels found in two control populations consisting of 246 individuals representing the adult general population and 143 patients with benign pulmonary disorders. The frequency of serological atopy, ie the presence of specific IgE antibodies, was also significantly increased in the cancer population as compared to the controls. In contrast, the incidence of possible clinical atopy was about 5x higher in the general population than in the cancer group. Patients with bronchial carcinoma typed as adenocarcinoma had the best prognosis and also had nonelevated IgE levels in contrast to patients with bronchial carcinoma typed as squamous cell carcinoma, small or large cell carcinoma. The favorable prognosis with nonelevated IgE levels also was demonstrated in patients with squamous cell carcinoma. It is suggested that the elevated IgE levels in bronchial carcinoma reflect impaired cellular immunity. (Author abstract) (25 Refs)

39. IMMUNOHISTOLOGIC EVIDENCE FOR THE ROLE OF ANTIBODY AND MACROPHAGES IN REGRESSION OF THE MURINE T1699 MAMMARY ADENOCARCINOMA.

Key M, Haskill JS
Cancer Metastasis and Treatment Lab., NCI Frederick Cancer Res. Center, Frederick, MD, 21701
Int J Cancer; 28(2):225-236 1981

The regression or progression of the T1699 murine mammary adenocarcinoma was analyzed with histologic and immunohistologic techniques to determine the tissue distribution of both macrophages and antitumor antibody. Changes in integrity of tumor blood vessels were apparent during tumor growth and regression. Tumors at early stages of growth were invaded in the capsule by multiple vascular branches which later permeated the tumor. Following the appearance of anti-tumor antibody in the serum, these vessels often showed immune complex deposition which preceded vessel leakage, destruction and hemorrhage. After these changes, tumor cells appeared coated with antibody. Macrophages appeared predominantly in the tumor capsule during early stages of tumor growth, while at later stages they were observed within tumors most prominently near the edge of growing hemorrhagic and necrotic areas. As tumors regressed, connective tissue septation lined by macrophages became apparent. Phagocytosis of seemingly intact tumor cells was common and appeared to account for much of the loss in tumor cell numbers. In immunosuppressed animals (ATXBM, 450R) in which tumor progression always occurred, the above features were markedly diminished or absent. This model emphasizes the interplay of many factors in tumor regression. These include immune complex deposition, blood vessel destruction, macrophage infiltration and connective tissue development, all of which are associated with tumor regression and seem to be infrequent and/or inconsequential during progressive tumor growth. (Author abstract) (39 Refs)

40. SPONTANEOUS AND ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY BY LYMPHOCYTE SUBPOPULATIONS IN PERIPHERAL BLOOD AND SPLEEN FROM ADULT UNTREATED PATIENTS WITH HODGKIN'S DISEASE.

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Clin Exp Immunol; 45(1):205-214 1981

Subpopulations of lymphocytes in the peripheral blood and spleen from adult untreated patients with Hodgkin's disease were studied for spontaneous (SCMC) and antibody-dependent cellular cytotoxicities (ADCC). Peripheral blood from 7 of 24 patients demonstrated abnormally low T cell-mediated SCMC when compared to age- and sex-matched healthy controls. Only two of these patients also demonstrated low T cell ADCC and non-T cell-mediated SCMC and ADCC. T cell ADCC in the peripheral blood of patients with involved spleen was significantly higher (p less than 0.05) when compared to those in whom spleen was not involved. When SCMC and ADCC were compared between peripheral blood and splenic lymphocytes with regard to involvement of spleen by Hodgkin's disease, non-T cell SCMC in the involved spleen was significantly lower (p less than 0.05) than their peripheral blood non-T cell SCMC. SCMC and ADCC tended to be higher in patients with Stages III and IV of Hodgkin's disease when compared to those with Stages I and II. However, the differences were not statistically significant. No direct relationship was observed between T cell SCMC or ADCC and the proportion of T cells with IgG Fc receptors (Tgamma). The significance of these observations is discussed. (Author abstract) (56 Refs)

41. SUBCLASS-RESTRICTED HUMAN IGG-ANTIBODIES INVOLVED IN ANTIBODY-DEPENDENT CELL-MEDIATED CYTOTOXICITY (ADCC) AND INDIRECT IMMUNOFLOURESCENCE (IF) (MEETING ABSTRACT).

Hadam MR, Staudhammer R
Institute of Immunology, Munich, W. Germany
Immunobiol; 159(1/2):187 1981

Melanoma patients' sera were investigated for IgG antibodies against cultured human melanoma cells by IF and ADCC using purified human lymphocytes as effector cells. Emphasis was laid on the immunochemical characterization of the antibodies involved rather than on the definition of specificity. Double-IF using TRITC-labelled R-F(ab')(2)-anti-human IgG in combination with FITC-Protein A brought up a number of sera containing primarily antibodies of the IgG3 subclass. These sera were not reactive in ADCC. Sera with high reactivity in ADCC were rare; they could not be shown to contain significant amounts of antibodies reactive in IF. However, preparative gel chromatography of selected sera on Sephacryl S-300 demonstrated ADCC-activity confined to the 7s-IgG peak. Affinity chromatography of ADCC-inducing sera on protein A sepharose related all activity to the bound fraction, ie IgG1, 2, 4, (5/5). However, in 7/7 isolated IgG3 proteins from IF-positive sera no ADCC could be found, whereas those antibodies were still highly active in IF. Furthermore, no ADCC-activity could be induced by removal of aggregates via ultracentrifugation or by sensitization of target cells. From these data we conclude that human IgG3 when bound to tumor cell targets as detected by IF is unable to mediate ADCC with human lymphocytes as effectors cells. Apart from the IgG3 nature of the antibodies, distinct density requirements of the antigen or variations in lateral movement within the membrane may as well account for the lack of ADCC. For induction of ADCC we propose that only some human IgG subclasses, presumably solely IgG2, will produce ADCC with human lymphocytes. This IgG subclass is the only one for which induction of ADCC against nucleated targets has been described, although all four IgG subclasses have repeatedly been shown to be inhibitory when added to an ongoing ADCC reaction. This might be indicative of differing prerequisites for inhibition or triggering itself. Along with that hypothesis, ADCC could be interpreted as a sort of anti-polysaccharide response which is known to be restricted to the IgG2 subclass in man. Only the repetitive nature of the polysaccharide antigens may allow sufficient effectotarget-cell interaction needed for ADCC to occur. (no Refs)

42. BINDING OF MONOCLONAL ANTIBODIES TO HUMAN BREAST CANCER (MEETING ABSTRACT).

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4th Annual San Antonio Breast Cancer Symposium, Nov 6-7, 1981, San Antonio, Texas Cancer Therapy and Research Center of South Texas; 1981

Monoclonal antibodies which react specifically with human breast cancer cells have been generated using hybridoma technology. Two hybridoma cell lines, H59 and H71 were established from the fusion between spleen cells immunized with ZR-75-1 cells, a cloned human breast cell line, and murine myeloma cells. H59 and H71 secrete IgMkappa antibodies which react with glandular estrogen receptor positive breast cancer cell ines, but not with more undifferentiated breast cancer cell lines. Only H71 antibody reacts with a well differentiated breast cancer cell line, T47D, which does not contain estrogen receptors. The H59 and H71 antigens have been isolated by indirect immune precipitation. H59 antigen is a protein complex composed of 2 peptides of approx 30,000 daltons; H71 antigen consists of 2 peptides which are about 28,000 and 2 that are 45,000 daltons. H59 antibody bound to fixed cryosections from 45 of 73 (61.6%) patients with breast cancer; H71 bound to 26 of 53 (49%). Thirty-four percent of specimens reacted with both antibodies while 28.3 percent bound neither antibody. H59 may bind a subset of estrogen receptor positive tumors, whereas H71 bound specimens which do and do not contain estrogen receptors. Both antibodies bound specimens which were progesterone receptor positive and negative. Both antibodies react with most specimens from fibrocystic disease and fibroadenomas. Since both antibodies were identified in differentiated breast cancer cell lines, and benign breast disease, the presence of the antigens in a breast cancer might indicate a more differentiated tumor and be associated with a better prognosis. (no Refs)

43. STRUCTURAL CHARACTERIZATION OF HUMAN MELANOMA-ASSOCIATED ANTIGEN P97 WITH MONOCLONAL ANTIBODIES.

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J Immunol; 127(2):539-546 1981

Monoclonal antibodies were used to study p97, a human melanoma-associated antigen (MAA). Four hybridomas, designated 4.1, 96.5, 118.1, and 8.2, were obtained by fusing mouse myeloma cells with spleen cells from mice immunized with human melanoma cells. Antibodies 4.1 and 8.2 were IgG1; antibodies 96.5 and 118.1 were IgG2a. Sequential immunoprecipitation (IP) and sodium-dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) showed that all four antibodies recognized the same 97 kilodalton (kD) protein. Binding studies with 125I-labeled antibody showed that antibodies 4.1 and 96.5 bound the same epitope , p97a. Antibodies 118.1 and 8.2 defined epitopes p97b and p97c, respectively. Six monoclonal antibodies (M17, L1, L10, R10, I12, and K5) specific for gp95, a 95 kD melanoma cell surface glycoprotein were also tested. Sequential IP showed that these antibodies bound p97; p97 and gp95 are thus identical. Binding studies showed that antibody M17 bound epitope p97a, and antibodies L1, L10, and R19 bound epitope 97c. Antibodies I12 and K5 defined two other epitopes, p97d and p97e, respectively. SDS-PAGE under on reducing conditions indicated that p97 is monomeric, probably with intrachain disulfide bonds. Cell-surface labeling of sialic acid residues and neuraminidase digestion showed that p97 is a sialoglycoprotein. Digestion of p97 with papain or trypsin produced a stable 40 kD fragment, which expressed epitopes p97a, p97b, and p97c, but not p97d or p97e. (Author abstract) (35 Refs)

44. DECISIVE PROGRESS IN MARKER STUDIES OF NORMAL AND MALIGNANT CELLS: MONOCLONAL ANTIBODIES AND FLOW MICROFLUOROMETRY.

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Arch Fr Pediatr; 38(5):369-374 1981

Biological markers indicative of various lymphocyte pathologies, particularly their neoplastic transformation (lymphomas and leukemias) are discussed. The role of serological analysis in the study of cell surface markers is described along with a discussion of the difficulties encountered with classic serological analysis. Lymphocyte hybridization and the development of monoclonal antibodies are described along with the detection of the binding of antibodies on cell surface antigens by flow microfluorometry. The determination of the levels of T lymphocyte differentiation and the identification of T cell subpopulations through the use monoclonal antibodies is described. The possibility of using monoclonal antibodies to define the tumor surface antigens in man is is discussed. The antigenicity of non-T, non-B acute lymphoblastic leukemia and the therapeutic implications of this form of leukemia are discussed. (26 Refs) (In FRE)

45. BIOLOGICAL ACTIVITY OF THE ANTITUMOR PROTEIN NEOCARZINOSTATIN COUPLED TO A MONOCLONAL ANTIBODY BY N-SUCCINIMIDYL 3-(2-PYRIDYLDITHIO)-PROPIONATE.

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Biochem Biophys Res Commun; 101(2):599-606 1981

The successful crosslinking of neocarzinostatin (NCS) to an IgG1 monoclonal antibody yielding hybrid proteins with biological activity is described. IgG1 is a myeloma protein obtained from the ascites fluid of pristan-treated BALB/c mice. The heterobifunctional reagent N-succinimidyl 3-(2-pyridyldithio)-propionate was used. It was shown that NCS can be linked to monoclonal antibody without loosing its biological activity as measured by the degradation of T2-DNA and bacteriostatic action. Since the hybrid protein still binds to protein A, a drastic change of antibody integrity is unlikely. The antigen binding ability of the hybrid protein, however, remains to be shown. (22 Refs)

46. COMMON NEUROECTODERMAL ANTIGENS ON HUMAN MELANOMA, NEUROBLASTOMA, RETINOBLASTOMA, GLIOBLASTOMA AND FETAL BRAIN REVEALED BY HYBRIDOMA ANTIBODIES RAISED AGAINST MELANOMA CELLS.

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Eur J Immunol; 11(6):450-454 1981

The hybridoma system has been utilized to produce antibodies to characterize the cell surface antigens on human melanoma cells. On initial screening, two antibodies derived by the fusion of mouse myeloma cells (SP2/O-Ag14) and splenocytes from a mouse immunized with a melanoma cell line (CaCl 78-1) showed cross-reactivity with 10 melanoma cell lines and did not react with any of 4 epithelial cancer lines, or 4 normal adult fibroblast lines. However, because of reactivity with two neuroblastoma cell lines, additional testing with other neuroectodermal derivatives was carried out and revealed a broad cross-reactivity among melanomas, neuroblastomas, retinoblastomas and glioblastomas and against antigens shared by fetal but not adult brain. Thus, these results indicate the existence of common neuroectodermal antigens on melanoma cells. Before melanoma specificity can be claimed for, an antibody reactivity with nonmelanoma cells bearing these neuroectodermal antigens should be excluded. (Author abstract) (21 Refs)

47. ABSENCE OF COMMON ALL ANTIGEN ON NORMAL BIPOTENT MYELOID, ERYTHROID, AND GRANULOCYTE PROGENITORS.

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Blood; 58(2):333-336 1981

The presence of the common acute lymphoblastic leukemia antigen (CALLA) on leukemic cells from the great majority of patients with non-T-cell acute lymphoblastic leukemia and chronic myelogenous leukemia in blast crisis suggests that CALLA could be a differentiation antigen expressed by normal lymphoid and myeloid stem cells. Treatment with a murine monoclonal anti-CALLA antibody and complement lysed CALLA-positive leukemic cells quantitatively, whereas similar treatment of nucleated cells from peripheral blood and bone marrow failed to affect the expression, in semisolid culture, of CFU-G/E, BFU-E, CFU-E, or CFU-C. These data suggest that CALLA is not a normal differentiation antigen of the myeloid bipotent cell or its committed progenitors. (Author abstract) (20 Refs)

48. CHANGES IN ANTITUMOR IMMUNITY AFTER SURGICAL AND CRYOSURGICAL TREATMENT OF TUMOR AND EFFECTS ON NONSPECIFIC IMMUNOSTIMULANTS. EXPERIMENTAL STUDIES USING A RAT TRANSPLANTABLE MAMMARY TUMOR.

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Gifu Daigaku Igakubu Kiyo; 29(2):228-277 1981

Sprague-Dawley rats in which tumors were induced by a metastasizing rat mammary tumor, MRMT-1, were examined for the effects of surgery, cryosurgery and nonspecific immunostimulants on antitumor immunity. Of the rats in which the tumor was surgically excised 2 wk after inoculation and did not have metastasis, antitumor immunity evaluated by footpad assay showed a peak 4 wk earlier than the rats with unexcised tumors. The nonspecific immunostimulants klebsiellar polysaccharide (PSK), OK-432 and levamisole (LMS) given repeatedly for 1 wk inhibited tumor growth and, except for PSK, lymph node metastasis. In rats in which tumors had been inoculated in the back 2 wk earlier, 81.8% of the regional lymph nodes harbored tumor cells. The incidence of established lymph node metastasis in rats whose tumors had been excised 2 wk after inoculation was 51.6%. Immunostimulants given preoperatively caused no significant change in mortality from metastasis or survival time, but large amounts given postoperatively worsened the disease and reduced footpad reactivit Splenectomy combined with tumor excision caused further improvement. The effects of therapy were similar in the rat treated by cryosurgery and surgical excision, suggesting tha the immunosuppressive effect of an intense cryosurgical insul was counteracted by cryogenically induced immunity. In th early postoperative stage, specific cell-mediated immunity wa stronger in the surgical excision group than in the cryosurger group, while the reverse was true in the late postoperativ stage. Antibody-mediated immunity was significantly stronge in the cryosurgery group than in the surgical excision group wk after surgery. (81 Refs) (In JPN)

49. ANALYSIS OF CELL-SURFACE ANTIGEN OF HAIRY CELL LEUKEMIA (HCL).

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Igaku Ayumi; 116(1):29-31 1981

One patient with cell surface Ig-positive HCL and another patient with HCL shown to have B cell markers by immunoprecipitation with anti-HCG and anti-B serum were seen. An antiserum specific for hairy cells (AHCS) was obtained by immunizing rabbits with 2 x 10(7) hairy cells iv. The absorbed AHCS for both patients diluted 80-160x produced 100% fluorescein isothiocyanate-stained cells, but peripheral blood (T, B cells) and the two B-cell lymphoid leukemias were not responsive. Some tonsil B cells responded with fluorescence of 12-27%, but no T cells responded. Various leukemia cells other than the hairy cells barely responded to the lymphocytes, nor did they respond to the granulocyte or monocyte leukemia cells. The unabsorbed antiserum had four major peaks, with mol wt of 110,000-120,000, 94,000-96,000, 48,000-50,000, and 30,000-34,000 for I, II, III, and IV. In the absorbed AHCS, peaks II and IV disappeared, leaving only I and II. The antigen at peak III is considered to differ from histocompatibility antigen (HLA) because it is not absorbed by anti-HLA or anti-beta2m. This antigen is considered to be the one that is differentiated from that of B cells which characterizes the hairy cell. The antigen at peak IV was also obtained by adding anti-B serum to the B cell lysates and the peak IV antigen that disappeared was considered to be an Ia-like antigen on the hairy cell. Antisera obtained from the two HCL patients were shown to recognize the same antigen. (Author abstract) (12 Refs) (In JPN)

50. HLA-A,B ANTIGENS, IA-LIKE ANTIGENS, AND TUMOR-ASSOCIATED ANTIGENS ON PROSTATE CARCINOMA CELL LINES: SEROLOGIC AND IMMUNOCHEMICAL ANALYSIS WITH MONOCLONAL ANTIBODIES.

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J Immunol; 127(2):443-447 1981

Serologic and immunochemical analysis of the antigenic profile of the two human prostate carcinoma cell lines DU-145 and H494 with a battery of monoclonal antibodies has shown that both cell lines express HLA-A,B alloantigens and the 94,000 mol wt tumor-associated glycoprotein recognized by the monoclonal antibody 376.96S. In addition, the cell line H494 unexpected expresses Ia-like antigens, which are similar in their antigenic profile and structure to B lymphoid cell derived Ia-like antigens. Both Ia-like antigens and tumor-associated antigens can function as targets of cell-dependent lysis mediated by the corresponding monoclonal antibodies. (Author abstract) (29 Refs)

51. EVIDENCE FOR T CELL NATURE AND HETEROGENEITY WITHIN NATURAL KILLER (NK) AND ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY (ADCC) EFFECTORS: A COMPARISON WITH CYTOLYTIC T LYMPHOCYTES (CTL).

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J Immunol; 127(2):448-452 1981

Three monoclonal antibodies (Ab) to human T lymphocytes (9.3, 9.6, and 10.2), a monoclonal Ab to the human Ia antigen (7.2), and a monoclonal Ab recognizing a monocyte-associated antigen (OKM1) were used to characterize three cytolytic effector types: CTL, NK, and ADCC. Activity was measured after treatment with Ab plus C. T cell antigen 9.3 was expressed on all CTL but gave only minimal reduction in NK or ADCC activities in the presence of C. T cell antigen 10.2 was expressed on all CTL and, in the presence of C, reduced by one-half the NK or ADCC activities. CTL were heterogeneous in expression of 9.3 and 10.2 antigens on days 5 and 7 of MLC, whereas all CTL were positive on day 9. T cell antigen, closely associated with the E receptor, was found on all CTL and NK cells and the great majority of ADCC effectors. Our finding with 9.6 confirms by independent and more direct means the findings of others that NK and ADCC effectors reside within the sheep rosetting population. Further experiments were performed with Ab in the absence of C. Ab 9.6 was able to partially block CTL and NK activities but not ADCC effectors. Ab OKM1 was unable to block NK or ADCC activities, despite its ability in the presence of C to ablate the majority of NK and ADCC lytic activity. Ab 9.3 was capable of blocking CTL activity but not NK or ADCC activity. Treatment with Ab 10.2 had no blocking activity against CTL, NK, or ADCC effectors. In sum, these results indicate that NK and ADCC effectors express, at least in part, differentiation antigens recognized by three monoclonal Ab to T lymphocytes, thus suggesting that some of these effectors may derive from a T cell origin. Although NK and ADCC effectors were identical based on cell surface phenotype, Ab blocking experiments could distinguish these activities. (Author abstract) (37 Refs)

52. SEROTHERAPY OF LEUKEMIA L1210 WITH SPECIFIC MONOCLONAL ANTIBODY (MEETING ABSTRACT).

Testorelli C, Quadrio C, Manera C, Nicolin A
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Tumori; 67(2,Suppl.A):169 1981

Our laboratory has produced a monoclonal antibody-secreting hybrid line (L1) endowed with high 'in vitro' cytotoxic activity compared to L1210 leukemia cells. The specificity of this effect was demonstrated by means of a broad screening carried out on cells of normal adult and fetal tissues and neoplastic cells of numerous murine tumors. Experiments with serotherapy in mice with leukemia L1210 subjected to various treatment schemes with L1 and rabbit complement have shown that monoclonal antibody is incapable of exerting any therapeutic effect. Experimental studies designed to study the in vivo effects of L1 yielded the following results: 1) L1 antibody administered in vivo is capable of localizing itself in the tumor and binding itself to the tumor cells; 2) it is possible to detect variable amounts of the antigen defined by L1 antibody, correlated with the degree of tumor development in the ascites of L1210-bearing mice; 3) the ascites of L1210-bearing mice has an anticomplement activity which depends on complement dilution; 4) L1 antibody has a modulating effect on the expression of the antibody it defines. (no Refs) (In ITA)

53. THE BIOCHEMISTRY OF TUMOR ASSOCIATED GANGLIOTRIOSYLCERAMIDE AND THE USE OF THIS GLYCOLIPID AS A TARGET FOR ANTIBODY DEPENDENT, AVIDIN MEDIATED DRUG KILLING OF TUMOR CELLS.

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Diss Abstr Int (B); 41(11):4062-B 1981

The use of antibodies to direct drugs specifically to tumor cells, in order to avoid toxic effects on normal tissue, has been hindered by: (I) the lack of chemically-defined, tumor-specific antigens to use as targets, (II) the absence of high-titered, tumor-specific antibodies, and (III) the loss of antibody or drug activity following antibody-drug conjugation. A novel indirect targeting system was designed that minimized the loss of antibody and drug activity and that introduced the potential for amplifying the number of drug molecules that could associate with cells. Anti-gangliotriosylceramide was derivatized with biotin-N-hydroxy-succinimide with full retention of its hemagglutinating activity. Avidin was then used to bridge biotin substituted drugs to biotinyl antibody bound to cells. Biotinyl neocarzinostatin, biotinyl daunomycin and liposomes that contained actinomycin D, were synthesized and directed to cells by this procedure. Successful targeting and killing of tumor cells expressing gangliotriosylceramide was only observed with biotinyl neocarzinostatin. Targeting required the presence of biotin on both the antibody and the drug. Furthermore, absorption of biotinyl antibody with guinea pig RBC, abrogated targeting. Actinomycin D was targeted to cells in liposomes prepared from biotinyl phosphatidylethanolamine, lecithin and cholesterol. Alternatively, avidin was covalently linked to liposomes prepared with sialyllactosylceramide by reductive amination (after the periodate oxidation of the liposomes). Liposome targeting was successful, but the ultimate delivery of encapsulated drug to the cell was not. In vivo therapy of L5178c127 tumors was initiated with biotinyl neocarzinostatin. Forty percent of the tumor bearing animals treated with biotinyl-antigangliotriosylceramide (IgM monoclonal antibody) + avidin + biotinyl neocarzinostatin have survived. All animals treated with biotinyl IgM alone or the combination of, unsubstituted IgM + avidin + biotinyl neocarzinostatin, have died. Monoclonal IgG3 anti-gangliotriosylceramide was effective by itself in the treatment of this tumor. (no Refs)

54. CLINICAL AND IMMUNOLOGICAL SIGNIFICANCE OF AUTOLOGOUS SERUM ANTITUMOR ANTIBODIES IN TONSILLAR CARCINOMA (MEETING ABSTRACT).

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Eur Surg Res; 13(1):96 1981

Sera from 53 patients with various stages of tonsillar carcinoma were analyzed for autologous and allogeneic antitumor membrane antibodies. The patients were followed in 2 monthly intervals after operation plus irradiation, irradiation only or chemotherapy. In all patients circulating autologous antitumor antibodies could be detected. The antimembrane antibodies belonged to the IgG class only. In swaps taken 4 wk after operation no tumor cells could be detected by immunofluorescence (IF) using preoperative sera. In case of recurrency positive (tumor) cells showed IF 3-6 mo before local reappearance of the tumor could be recognized clinically. Patients having such positive cells in their swaps cytology die usually from widespread disease within 1 yr showing constant positive IF. In patients with progressed stages, where only irradiation or chemotherapy (bleomycin or cis-platinum) could be applied these IF-positive cells are reduced after therapy. However, they never disappear completely and increase again under recurrency. At time when IF appears first after operation no malignant cells can be recognized by Papanicolaou staining. Incubation with monoclonal anti-Ia antibodies indicate that some cells carry Ia antigens on their surface. Detection of IF-positive tumor cells in swaps by the use of autologous antibodies seems to be a method that allows to recognize early recurrencies of tonsillar carcinoma. Though the function of these antibodies in tonsillar carcinoma is still unclear they seem to be of prognostic value providing useful tools to reduce further invasive diagnostic methods. (no Refs)

55. STUDIES ON NATURAL KILLER CELL AND ANTIBODY DEPENDENT CELL MEDIATED CYTOTOXICITY IN GNOTOBIOTIC AND CONVENTIONAL C3H/HECR MICE.

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Diss Abstr Int (B); 41(11):4061-B 1981

Normal and Poly I:C stimulated levels of murine NK and ADCC activities were measured using a short term in vitro 51Cr release assay in which spleen cells prepared from both germfree and conventional C3H/HeCr inbred mice were used as a source of effector cells and YAC-1 Moloney virus induced leukemic cells, RL 1 radiation induced by lymphoma cells, and nucleated chicken RBC were used as target cells. For proper statistical analysis, the mice were sacrificed according to two experimental designs at 6, 12, 16, 24, and 42 wk of age. The results of this study indicated that the presence of a viable murine microflora is not required for the age-dependent expression of either NK or ADCC activity, that the presence of such a microflora modulates both the normal and potential level of NK and ADCC activity expressed by conventional mice, and that the absence of such a microflora alters the quantitative but not qualitative expression of NK and ADCC cytotoxicities in the experimental mouse strain. Additional characterization studies indicated that the spleen cell population responsible for the observed ADCC activities consisted of nonadherent nonphagocytic, Ig cells that could also express low levels of Thy-1 surface determinants. The effector cells responsible for the observed NK activities were found to be nonadherent, nonphagocytic, Ig cells that would express Thy-1 membrane determinants when stimulated in vivo with Poly I:C. Together, the results of this study suggest that germfree inbred mice can be used as controlled model systems for the study of the biological implications of NK and ADCC cytotoxicities. (no Refs)

IMMUNOGLOBULIN STRUCTURE AND SYNTHESIS

56. IGE ANTIBODY PRODUCTION IN GUINEA PIGS TREATED WITH CYCLOPHOSPHAMIDE.

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J Immunol; 127(3):1067-1070 1981

Guinea pig anaphylactic responses usually involve IgG1 antibodies. Although IgE antibody production has been accomplished, a reliable and sustained method for production has not been described. We have investigated a method of enhancing IgE antibody production in guinea pigs. The criteria for IgE production were homologous passive cutaneous anaphylaxis (PCA) antibody activity that passed an affinity column of rabbit anti-guinea pig IgG1, heat lability (56 C for 4 hr), and a long sensitization period in skin (7 days). Hartley guinea pigs were primed and boosted monthly with 1 ug Picryl-Ascaris plus 1 mg of alum ip. Some Hartley guinea pigs also received cyclophosphamide (250 mg/kg) before the first boost. English short-hair guinea pigs (previously shown to be good IgE producers) were immunized similarly but received no cyclophosphamide. Hartley animals receiving no cyclophosphamide inconsistently made low titered IgE anti-hapten antibody (1:100). Fifteen of 15 Hartley animals that received cyclophosphamide had high titers (1:2000) of IgE anti-hapten antibody. English short-hair animals had moderate titers (1:400), and not all animals responded. Thus, cyclophosphamide converted IgE nonresponder Hartley guinea pigs to uniformly high responders. This method provides material to study the biologic properties of IgE in this species, and also provides a model to study the apparent suppression of IgE responses in Hartley guinea pigs. (Author abstract) (16 Refs)

57. THE INFLUENCE OF CYCLOPHOSPHAMIDE AND 6-MERCAPTOPURINE ON THE IGG1 AND IGG2 IMMUNE RESPONSE IN GUINEA-PIGS.

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Immunology; 44(1):61-66 1981

The purpose of this study was to investigate the effect of cyclophosphamide (CY) and 6-mercaptopurine (6-MP) on the production of the two Ig antibody subclasses in guinea-pigs. Following the id application of dinitrophenylated bovine gamma globulin (DNP20-BGG) emulsified in Freund's incomplete adjuvant (FIA) each animal was given CY or 6-MP, 10 mg per kg of body wt per day on days 1-7, and the DNP- and BGG-specific anaphylactic (IgG1) and lytic (IgG2) antibodies were determined. Only treatment with CY resulted in a significantly-depressed IgG2 anti-DNP immune response; 6-MP was not suppressive and caused a prolonged IgG2 anti-DNP production. Both substances showed a stimulatory effect on IgG1 anti-DNP antibody formation. The carrier-specific IgG1 and IgG2 antibody levels were suppressed completely by Cy but unaffected by 6-MP. After a booster injection of 1 mg BGG on day 86 the animals in the CY-treated group were not able to mount a secondary IgG2 anti-BGG immune response. In contrast, IgG1 anti-BGG production was strong and uninfluenced by CY treatment. (Author abstract) (21 Refs)

58. SPECIFICITY OF FC RECEPTORS FOR IGG2A, IGG1/IGG2B, AND IGE ON RAT MACROPHAGES.

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J Exp Med; 154(2):374-384 1981

Alveolar and peritoneal macrophages (M-phi) were obtained from Lewis and Brown Norway rats. The ability of M-phi to form rosettes with fixed ox RBC (Eo') coated with myeloma proteins of all Ig classes, and with fresh RBC (Eo) sensitized with rat IgG1 and IgG2, rabbit IgG and IgM, and mouse antibodies was measured. Rosettes were formed with Eo' coated with IgG1, IgG2a, IgG2b, and IgE myeloma proteins, but not with IgG2c, IgA, IgM, or IgD. Rosettes were also formed with Eo' coated with human IgG1, IgG3, IgG4, mouse IgG1, IgG2a, IgG2b, and rabbit IgG. Rosettes were formed with Eo sensitized with rat IgG1, IgG2, or rabbit IgG. No rosettes were formed with rabbit IgM or mouse IgA. M-phi treated with trypsin formed rosettes with IgG2a, but not with IgG1, IgG2b, or IgE. The IgG2a and IgE rosettes were inhibited only by rat IgG2a and IgE, respectively, indicating that they were class specific. IgG1 and IgG2b were not class specific. Apparently rat M-phi have at least three types of Fc receptors: (1) a rat IgG2a-specific, trypsin resistant receptor, (2) a rat IgE-specific, trypsin-sensitive receptor, and (3) a rat IgG1, IgG2b, and heterologous IgG-sensitive, trypsin sensitive receptor. (49 Refs)

59. DISTRIBUTION OF SURFACE, CYTOPLASMIC AND SECRETED IGG SUBCLASSES IN HUMAN LYMPHOBLASTOID CELL LINES AND NORMAL PERIPHERAL BLOOD LYMPHOCYTES.

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Scand J Immunol; 14(1):1-13 1981

Twenty-two IgG-positive lymphoblastoid cell lines and normal peripheral blood lymphocytes were studied for surface and cytoplasmic IgG, IgG subclasses, IgD and IgM, using monospecific fluorescein- and rhodamine-conjugated F(ab')2 antibody fragments, and for secretion by double antibody radioimmunoassay. Several parallel observations and several differences in IgG subclass expression were noted between cell lines and normal lymphocytes. Surface IgG2 was frequently expressed in normal IgG-positive lymphocytes but was seldom expressed in cell lines. Cell lines resembled normal IgG-positive lymphocytes in the frequent expression of cytoplasmic IgG3 and IgG4, often without secretion. Cell lines and normal lymphocytes both showed more frequent distribution of IgG and IgG subclasses in cytoplasm than in surface immunoglobulin, and often a discrepancy of surface versus cytoplasmic IgG subclass. A good correlation was noted between surface, cytoplasmic and secreted IgG1. Despite a predominance of IgG2 and IgG4 surface IgG subclasses, and IgG3 and IgG1 in cytoplasm, secreted immunoglobulins from normal lymphocytes in short-term culture showed a similar distribution of IgG subclasses to that seen in normal sera. Multiple expression of IgG subclasses was much more frequent in IgG-positive cell lines than in normal peripheral blood lymphocytes, both in surface and cytoplasmic IgG. (Author abstract) (16 Refs)

60. NEW MOUSE IMMUNOGLOBULIN A HEAVY CHAIN ALLOTYPE SPECIFICITIES DETECTED USING THE HYBRIDOMA-DERIVED IGA OF I/ST MICE.

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Immunogenetics; 13(6):475-481 1981

Immunizations of C57BL/6 and A mice with IgA derived from the I/St mouse strain yield alloantisera which detect two allotypic determinants of IgA. The two determinants display discrete strain distributions. The first, identified by the alloantiserum C57BL/6 anti-IgA of I/St strain hybridoma ID150, follows the Ighc haplotype, and the second, identified by the alloantiserum A anti-IgA of I/St strain hybridoma ID150, correlates with Ighc and Ighb haplotypes. Absorption with monoclonal IgM, which has the same idiotype as the ID150 IgA clone, removed idiotype-specific antibodies from both alloantisera. The remaining antibodies are directed against determinants associated with the alpha chain constant region, as shown by absorption with monoclonal IgA. By use of recombinant inbred strains of mice and mice congenic at the Igh locus, the loci controlling both Calpha allotypic determinants have been mapped to the Igh region on chromosome 12. (Author abstract) (16 Refs)

61. IMMUNOCHEMICAL STUDIES ON HETEROGENEITY OF IGD MYELOMA PROTEINS.

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Immunology; 43(4):717-722 1981

An antigenic heterogeneity among IgD myeloma proteins was tested by immunoelectrophoresis and double immunodiffusion in agar with four kinds of anti-delta (Fc) antisera produced by immunization with isolated Fc fragments of IgD myeloma proteins. According to antigenicity of the Fc fragment, IgD myeloma proteins were divided into two different groups. Anti-delta(Fc)-Tl(S.T.) antiserum, absorbed with the Y.S. myeloma protein or serum, either gave a faint precipitin line or failed to react against the isolated IgD myeloma proteins or sera. With the papain-digested IgD myeloma proteins and sera, anti-delta(Fc)-Tl antiserum either gave heavy precipitin lines or failed to react. Of twelve papain-digested sera containing IgD myeloma proteins tested, nine (75%) showed positive precipitin lines using anti-delta(Fc)-T1 antiserum. No relationship was found between the two groups of myeloma proteins with respect to IgD levels. SDS polyacrylamide gel electrophoresis of the IgD myeloma proteins (S.T. and Y.S.) showed no difference in the mol wt of the whole myeloma proteins, and their light and heavy chains. Polyacrylamide gel electrophoresis of the IgD myeloma proteins (S.T. and Y.S.), after treatment with papain, revealed almost the same patterns. (Author abstract) (5 Refs)

62. RECOGNITION OF H-2 DOMAINS BY CYTOTOXIC T LYMPHOCYTES.

Weyand C, Hammerling GJ, Goronzy J
Institut fur Immunologie und Genetik, Deutsches Krebsforschungszentrum, Heidelberg, Im Neuenheimer Feld 280, 6900 Heidelberg, W. Germany
Nature; 292(5824):627-629 1981

H-2Kk determinants defined by monoclonal antibodies are concentrated in the H-2Kk molecule in two spatially separated polymorphic domains, ie, clusters A and B. No monoclonal antibody tested completely blocked target cell lysis by H-2Kk-specific alloreactive cytotoxic T lymphocytes (CTLs) from DBA/2 mouse splenocytes. However, a mixture of the antibodies plus a polyvalent anti-H-2Kk antiserum resulted in almost complete inhibition of target cell lysis, suggesting the existence of different CTL clones with specificity for distinct H-2 determinants. Monoclonal antibodies to cluster B were much more efficient in target inhibition than antibodies to cluster A, indicating the more CTL clones were reactive against cluster B determinants than against cluster A determinants. In an H-2 restricted system, CBNA splenocytes were sensitized in vitro with trinitrophenyl (TNP)-conjugated CBA spleen cells, and their cytolytic activity was determined on TNP-conjugated H-2K target cells. Again individual monoclonal antibodies blocked only a fraction of the CTL effector population, whereas a mixture of monoclonal antibodies or a polyvalent antiserum again Kk almost completely prevented lysis. These results showed that the CTLs can recognize TNP in conjugation with different H-2 determinants, ie, one H-2Kk molecule carries greater than one restriction site. The blocking capacity of cluster B antibodies was also greater than that of cluster A antibodies in this system. (9 Refs)

63. PRESENCE OF STRUCTURALLY ABNORMAL MOLECULES IN MONOCLONAL G IMMUNOGLOBULINS IN HUMAN MYELOMAS.

Malati T, Gupta RM, Chakravorty M
(c/o Gupta) Dept. Pathology, Inst. Medical Sciences, Banaras Hindu Univ., Varanasi 221005, India
Indian J Med Res; 73:930-937 1981

Monoclonal IgGs were isolated from the sera of seven patients with multiple myeloma by ammonium sulfate precipitation and DEAE cellulose column chromatography. Analysis of incidence of class and light chain type showed that three monoclonal proteins were IgG1 type K, three IgG1 type L and one IgG2 type L. Biochemical and biophysical studies revealed the presence of subnormal molecules in three out of seven cases. In one case, a rarely reported aggregated molecule of IgG having 10.32 S value was observed, while in another, a minor peak of a low mol wt IgG of 4.83 S was observed and in the third case, the entire myeloma protein was of low S value 3.94. No antibody activity could be detected against a variety of antigens tested for, including common human commensal and pathogenic flora. Further, there was a preponderance of lambda light chain monoclonal immunoglobulins. These observations lend support to the belief that the plasma cell malignancy in humans may result from genetic predilection rather than from chronic bacterial stimulation. (Author abstract) (23 Refs)

64. POKEWEED MITOGEN-INDUCED GENERATION OF IMMUNOGLOBULIN-SECRETING CELLS IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA (MEETING ABSTRACT).

Rohl H, Enders B, Herrmann F, Teichmann H, Sieber G
Department of Haematology, Free University of Berlin, Berlin, W. Germany
Immunobiol; 159(1/2):130 1981

In the present study we have investigated the functional capacity of peripheral blood mononuclear cells from patients with chronic lymphocytic leukemia (CLL) to transform into immunoglobulin-secreting cells (ISC). After stimulation with Pokeweed mitogen (PWM) single ISC were enumerated in a reverse hemolytic plaque assay. Venous blood was taken from 41 patients with hematologically and histologically confirmed B-CLL. Lymphocytes from 36 patients who had markedly increased numbers of peripheral blood cells were found to be unable to generate ISC thus indicating that the leukemic B cells can not be activated. To exclude the possibility that the unresponsiveness was not due to a relative dilution of T helper cells, isolated B cells from the patients were cultured together with T cells from normal subjects. These experiments revealed that the unresponsiveness is indeed caused by an intrinsic defect of the leukemic cells. On the other hand, isolated T cells from CLL patients were found to be functionally normal helper cells when cocultured with normal B lymphocytes. However, only 5 patients who had all relatively low peripheral lymphocyte counts exhibited a significant response to PWM. Surprisingly, two of these patients had a severe antibody deficiency. In these two patients the effect of chemotherapy could be studied: the reduction of the peripheral lymphocytes resulted in a parallel and proportional increase in the number of ISC which was remarkably not followed by an increase in serum immunoglobulin levels. This finding suggests a normal B cell population present at least in some patients thus indicating that the immunodeficiency which is characteristic for CLL is not always due to an absence of functionally normal B lymphocytes but to cellular or humoral immunosuppressive mechanisms. (no Refs)

65. MOLECULAR ANALYSIS OF IMMUNOGLOBULIN GENE VARIANTS.

Choi EM
University of California, Los Angeles, CA
Diss Abstr Int (B); 42(1):69-B 1981

MPC-11 mouse myeloma cells synthesized a normal kappa (k) light chain immunoglobulin and a variant k light chain fragment. The k fragment contains a hydrophobic precursor region joined directly to the k constant region (Ck) but lacks a variable region. The precursor region sequence of the k fragment is different from that of the full-length light chain. The full-length light chain and k fragment are encoded by separate messenger RNA (mRNA) species. Investigations on MPC-11 cells were undertaken in order to understand how the abnormal k fragment mRNA was generated. It is shown that the k fragment mRNA is formed from an aberrantly rearranged immunoglobulin gene through an abnormal RNA splicing event. (no Refs)

66. MEMBRANE IMMUNOGLOBULINS OF SPONTANEOUS B LYMPHOMAS OF AGED BALB/C MICE.

Laskov R, Kim JK, Woods VL, McKeever PE, Asofsky R
The Hubert H. Humphrey Centre for Experimental Medicine and Cancer Res., The Hebrew Univ.-Hadassah Medical Sch., Jerusalem, Israel
Eur J Immunol; 11(6):462-468 1981

Four cell lines derived from spontaneous BALB/c B lymphoma tumors were analyzed with regard to the type of their membrane immunoglobulins (Ig). Using lactoperoxidase iodination of membrane proteins combined with immunoprecipitation and electrophoresis on polyacrylamide gel, three of these cell lines (X16c, L10A and K46) were found to express the monomeric form of IgM and IgD as well as half molecules. One cell line (M12) lacked both IgM and IgD. The apparent mol wt of the lymphoma mu chain was about 80,000 and exceeded the mol wt of 75,000 determined for mu chains secreted by myeloma cells. The mol wt of the delta heavy chain was found to be 66,000. Immunofluorescence showed that the L10A and

X16c lines expressed lambda light chains on their cell surface. Another Ig-bearing cell line (K46) expressed both lambda and chi chains. Thus, three out of the four B lymphomas examined expressed both IgM and IgD with light chains of the lambda type. These results, together with our previous findings which demonstrate the presence of Ia and Fc receptors on the same cells, indicate that spontaneous B lymphomas in BALB/c mice are the malignant counterpart of mature B lymphocytes. (Author abstract) (39 Refs)

67. DOUBLE LIGHT-CHAIN PRODUCTION BY LEUKEMIC CELLS OF COMMON CLONAL ORIGIN: A CASE REPORT WITH REVIEW OF PERTINENT LITERATURE.

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Bronx-Lebanon Hosp. Center, 1276 Fulton Ave., Bronx, NY, 10456
Am J Hematol; 11(1):93-98 1981

We are reporting the first case of acute lymphoblastic leukemia whose individual leukemic cells produced both kappa and lambda light chains, without any heavy chains, as demonstrated by double immunofluorescent staining. This case together with cases of lympho-plasmatic neoplasia reported in the literature indicates that cells of a single clone are capable of producing more than a single class of light and/or heavy chains. (Author abstract) (21 Refs)

68. A HYPOTHETICAL SPACE-FILLING MODEL OF THE V-REGIONS OF THE GALACTAN-BINDING MYELOMA IMMUNOGLOBULIN J539.

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Computer Center Branch, Div. Computer Res. and Technology, NCI, Bethesda, MD, 20205
Mol Immunol; 18(8):683-698 1981

J539 is an IgA myeloma protein whose V-region amino acid sequences and ligand binding for beta-1,6-galactosyl oligosaccharides have been determined in the past. Two hypothetical, three-dimensional models of this protein have now been constructed on a computer display system by modifying the known structures of McPC603. The J539 Fv is 11 amino acids shorter than McPC603, and its alpha-carbon backbone was formed by eliminating positions from McPC603 and rejoining the chains at three deletion sites in CDR-1 of VL and CDR-2 and-3 of VH. This maneuver was performed using a three-dimensional viewing system that displayed the amino acids with side chains in the regions around in break sites. The side chains of the amino acids in the model were oriented by a computer program that searched the available space for positions that did not make van der Waals contacts with neighboring atoms. Beta-1,6-Galactohexasoe has been fitted to the J539 combining site using the computer site using the computer display system. The terminal non-reducing sugar made close contacts with hydrogen bond accepting amino acids in CDR-2 of VH and oxygens of the third and fourth sugars were close to hydrogen bond accepting amino acids in CDR-2 of VH and oxygens of the third and fourth sugars were close to hydrogen bond accepting amino acids in CDR-1 and CDR-3 of VL. While the proposed structures are not unique solutions for J539 they present working models for further immunochemical experiments. (Author abstract) (43 Refs)

69. MECHANISM OF NEONATAL IDIOTYPE SUPPRESSION. III. DELAYED MATURATION OF PLASMACYTOMA STEM CELLS IN NEONATALLY SUPPRESSED HOSTS.

Kaus JA, D'Ottavio RM, Kohler H
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J Immunol; 127(2):509-513 1981

The immunologically altered state of the neonatally anti-idiotype suppressed mouse was investigated by using a myeloma tumor that secreted the suppressed idiotype. The splenic fragment culture technique developed by Klinman for the analysis of normal B cell precursors was adapted to measure the number of clonogenic tumor precursors. This technique was used to analyze clonogenic tumor cells growing in normal and neonatally suppressed hosts. HOPC-8 myeloma cells injected iv into normal or T15(H8) neonatally suppressed mice behaved differently, in vivo and in fragment culture. Serum idiotype in suppressed hosts rose rapidly after day 15 of growth in vivo, resulting in a final 35-fold difference in the idiotype amount between normal and suppressed hosts. The number of secreting tumor cells was determined by analyzing supernatants collected after 3 days of fragment culture. In splenic fragment cultures prepared from neonatally suppressed mice in which the tumor had grown for 7 or 14 days, no secreting cells were detected, whereas fragment cultures prepared identically from normal hosts did contain secreting cells. In contrast, neonatally suppressed mice that had received the HOPC-8 myeloma tumor 21 days earlier had a very large number of secreting tumor cells, whereas in normal mice 21 days after tumor transfer the number had decreased. When splenic fragment cultures from suppressed hosts having received tumor cells 14 days earlier were continued up to 6 days, a substantial number of newly producing foci were detected. The number of secreting cells detected by days 3 or 6 of culture was taken as a measure of clonogenic potential of tumor cells. The analysis of clonogenic tumor cells growing in normal and suppressed BALB/c mice correlates with the finding of delayed and increased in vivo secretion of myeloma protein. These data indicate that neonatally suppressed mice cause a delay in maturation of idiotype-committed plasmacytoma stem cells. (Author abstract) (20 Refs)

70. THETA POLYPEPTIDE PHENOTYPES OF LYMPHOID AND MYELOID CELL LINES CONTAINING RNA TRANSCRIPTS OF THE IMMUNOGLOBULIN CTHETA GENE.

Walker ID, Harris AW
The Walter and Eliza Hall Inst. Medical Res., Victoria 3050, Australia
J Immunol; 127(2):561-566 1981

We have examined whether polyadenylated-RNA molecules encoded by the immunoglobulin Cmu gene (Cu RNA) that have recently been shown to occur in mouse T lymphoma, myeloid tumor, and pre-B lymphoma cell lines are translated. Three T lymphoma, one myeloid tumor, and four Abelson lymphoma cell lines, all known to contain Cu RNA molecules, were examined for evidence of synthesis of mu polypeptides using radioimmunoassay, biosynthetic labeling, and immunoprecipitation techniques. No mu polypeptides were detected in any of the T lymphoma or myeloid cell lines, although mu-chains were readily detected in two B lymphoma lines known to contain small amounts of mu mRNA. Detection failure is unlikely to be the result of assay insensitivity and was not caused by lack of an appropriate antiserum reactivity or a requirement of mu-chains to be associated with immunoglobulin light chains. Proteolytic activity that might degrade newly synthesized mu polypeptides in these cell lines was not detected. In three of the four Abelson lymphoma cell lines containing Cu RNA, corresponding polypeptides were absent, although in the fourth they were easily detected, indicating that transcription of the Cu gene is not the sole determinant of whether a cell will synthesize the corresponding polypeptide. The parallel between the Cu RNA+, mu polypeptide- Abelson cell lines and the T lymphoma cell lines suggests that the onset of Cu transcription may occur in both T and B lineages before translational competence is acquired. (Author abstract) (35 Refs)

71. T CELL-REPLACING FACTOR (TRF)-INDUCED IGG SECRETION IN A HUMAN B BLASTOID CELL LINE AND DEMONSTRATION OF ACCEPTORS FOR TRF.

Muraguchi A, Kishimoto T, Miki Y, Kuritani T, Kaieda T, Yoshizaki K, Yamamura Y
Third Dept. Medicine, Osaka Univ. Medical Sch., Fukushima-ku, Osaka 553, Japan
J Immunol; 127(2):412-416 1981

IgG-secretion was induced in a human B blastoid cell line, CESS, by the addition of partially purified T cell-derived helper factor(s) (TRF), which had been obtained from PHA-stimulated human T cells. The number of IgG-producing cells in CESS cells reached its max level (10% of total cells) within 48 hr after the addition of TRF. TRF did not affect the proliferation of CESS cells and the block of cell proliferation with hydroxyurea did not inhibit the increase of IgG-producing cells, showing that TRF induced IgG-production in CESS cells without any requirement of cell division. TRF activity was completely removed by CESS cells but TCGF-activity in the same preparation was not absorbed with CESS cells. On the other hand, TCGF-dependent human killer cells absorbed TCGF activity but not TRF activity in the same preparation. The binding of 125I-labeled factor(s) on CESS cells was also demonstrated. These results showed that presence of acceptors for TRF on the surface of CESS cells and this cell line will provide useful means for the chemical characterization of acceptors and for the study of the mechanisms of the signal transmission through acceptors. (Author abstract) (27 Refs)

72. DETECTION OF J CHAIN IN LYMPHOMAS AND RELATED DISORDERS.

Laurent G, Delsol G, Reyes F, Abbal M, Mihaesco E
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Clin Exp Immunol; 44(3):620-528 1981

Lymph node specimens from 125 patients with malignant lymphomas and related disorders were studied by immunoperoxidase procedure for the presence of intracytoplasmic immunoglobulin (CIg) and J chain. CIg staining was present in 22/24 cases of lymphoplasmacytic-lymphoplasmacytoid lymphomas, and in 10/10 cases of extramedullary plasmacytomas and myelomas. In the majority of these cases J chain could be demonstrated in plasmacytoid or neoplastic plasma cells. In 21/36 cases of immunoblastic lymphomas, intracytoplasmic Ig staining was present. In only two of the 36 cases were the lymphomatous cells stained positively for J chain. J chain was not detected in other lymphomas such as lymphocytic lymphomas, follicular lymphomas, lymphoblastic lymphomas or in Reed-Sternberg cells or hairy cells. J chain was demonstrated in mature plasma cells and immunoblastic cells in hyperplastic lymph nodes, and in angioimmunoblastic lymphadenopathy. These findings show that J chain is not detectable in all B cell lymphomas even in the presence of CIg synthesis, irrespective of class. (Author abstract) (31 Refs)

HUMORAL IMMUNE BLOCKING FACTORS AND ANTIGEN-ANTIBODY COMPLEXES

73. IMMUNOTHERAPY OF MURINE LEUKEMIA. V. PROTECTION AGAINST FRIEND LEUKEMIA VIRUS-INDUCED IMMUNE COMPLEX GLOMERULONEPHRITIS BY PASSIVE SERUM THERAPY.

Sanfilippo F, Genovesi EV, Collins JJ
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JNCI; 67(3):703-717 1981

The development of immune complex glomerulonephritis in DBA/2 mice infected with Friend murine leukemia virus (F-MuLV) was compared with that in mice protected against virus-induced disease by administration of chimpanzee anti-F-MuLV antiserum (CaF-MuLV). Morphologic analysis of glomeruli from viremic (infected) normal chimpanzee serum-treated animals revealed significant renal disease within 2 wk following virus inoculation, with glomerular immune complex deposits and C-type viral particles seen by electron microscopy. Localization of F-MuLV envelope and core antigens (gp71 and p30, respectively) was also detected by immunofluorescence, as was murine IgG and C3. However, age-matched DBA/2 mice treated with CaF-MuLV antiserum alone or following F-MuLV inoculation showed no evidence of systemic disease and neither localization of F-MuLV antigens nor detectable virus particles. These data indicate that in addition to erythroleukemia, F-MuLV infection results in severe immune complex glomerulonephritis and that passive immunotherapy can protect susceptible mice from both aspects of viral pathogenesis. (Author abstract) (30 Refs)

74. ALBUMIN-IMMUNOGLOBULIN COMPLEXES IN HUMAN SERUM: CLASSIFICATION AND IMMUNOCHEMICAL ANALYSIS.

Eilat D, Fischel R, Zlotnick A
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Scand J Immunol; 14(1):77-87 1981

A complex between serum albumin and immunoglobulins was observed on immunoelectrophoresis in six patients. Two patients with multiple myeloma had monoclonal IgA-albumin complexes; one of these complexes was formed by covalent bonds and the other by noncovalent bonds. Four patients displayed non-covalent IgG-albumin complexes; of these, one had multiple myeloma, two had been treated with nitrofurantoin for prolonged periods, and one had diabetes mellitus. The IgG-albumin complex of the last patient was subjected to a detailed immunochemical analysis. The albumin-specific antibodies were isolated by affinity chromatography and analyzed, using a sensitive tritium labeling technique. The antibodies were polyclonal, complexed with serum albumin through their Fab portion, and showed a high specificity for the human albumin as compared with bovine and rabbit albumins. The serum albumin of two patients displayed an abnormal behavior in reduced SDS-polyacrylamide gel electrophoresis (PAGE). The abnormal albumins had an apparent mol wt of 52,000 and could react with rabbit anti-human serum albumin like the normal protein. No abnormal albumin could be detected in 20 other patients' sera, including nitrofurantoin-treated patients and normal controls. These findings suggest a possible role for an altered self-component in the triggering of a specific autoimmune reaction. (Author abstract) (23 Refs)

75. MULTIVARIATE ANALYSIS OF T-CELL FUNCTIONAL DEFECTS AND CIRCULATING SERUM FACTORS IN HODGKIN'S DISEASE.

Schulof RS, Bockman RS, Garofalo JA, Cirrincione C, Cunningham-Rundles S, Fernandes G, Day NK, Pinsky CM, Incefy GS, Thaler HT, Good RA Gupta S
Dept. Medicine, Div. Hematology and Oncology, George Washington Univ. Sch. Medicine, 2150 Pennsylvania Ave., N.W., Washington, DC, 20037
Cancer; 48(4):964-973 1981

A comprehensive immunologic and serologic analysis was performed on 31 untreated patients with Hodgkin's disease. Immune evaluations stressed T-cell functional activity and included traditional parameters (PHA responsiveness and delayed hypersensitivity skin reactivity), as well as newer functional assays [T-cell colony formation, chemotaxis, spontaneous and antibody-dependent cytotoxicity, and concanavalin A-induced suppressor cell activity (CISA)]. Serum factors included ferritin, prostaglandins, zinc, copper, immune complexes, and thymic hormone activity. Every patient exhibited at least one T-cell or serum abnormality. The greatest percentage of patients exhibited T-cell defects in chemotaxis (85%), colony formation (81%), and PHA reactivity (64%). Immune defects were more common with advanced disease but were not related to absolute T-cell or monocyte count, skin test anergy, or abnormalities of Tmu/Tgamma cell proportions. Linear relationships were identified among abnormalities in the three assays employing mononuclear cells (PHA, colony formation, CISA) which may have reflected the inhibitory influence of mon ocytes present in the mononuclear cell preparations. Low serum zinc correlated with marked impairment of T-cell chemotaxis. Elevated prostaglandins were associated with high PHA reactivity and with depressed colony formation. Elevated prostaglandins were associated with high PHA reactivity and with depressed colony formation. Our results indicate that many complex factors, including intrinsic T-cell defects, contribute to the impaired immunity associated with Hodgkin's disease. (Author abstract) (62 Refs)

76. ISOLATION OF IMMUNE COMPLEXES AND CHARACTERISATION OF THEIR CONSTITUENT ANTIGENS AND ANTIBODIES IN SOME HUMAN DISEASES: A REVIEW.

Jones VE, Orlans E
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J Immunol Methods; 44(3):249-270 1981

Methods for the isolation and purification of immune complexes (ICs) from biological fluids in amounts sufficient for analysis are reviewed. Existing methods and new possibilities for the identification of constituent antigens and antibodies and of other serum components almost invariably found in ICs, such as complement and rheumatoid factors, are examined. Topics discussed include sample handling, contaminants in preparations of ICs, concentration of ICs, isolation of ICs (staphylococcal protein A, binding to receptors on Raji cell membranes, binding to complement components and conglutinin, binding to anti-immunoglobulins and anti-complement3, and binding to antigen-specific antibody), reagents for dissociation and elution of ICs, and detection of antigen and antibody. (107 Refs)

77. C1Q BINDING ACTIVITY IN THE SERA OF PATIENTS WITH CHRONIC LUNG DISEASES.

Cooper KM, Moore M, Hilton AM
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Clin Exp Immunol; 45(1):18-28 1981

Sera from patients with chronic lung diseases were tested for the presence of immune complexes (ICs) by the 125I-C1q-binding assay. Contrary to earlier reports, modification of the test system by addition of heparin decreased rather than increased the ability of the test to discriminate between control and pathological sera. Using the unmodified system, elevated C1q-binding activity (C1qBA) was found in patients with asthma (18%), chronic bronchitis (18%), sarcoidosis (18%), fibrosing alveolitis (50%), bronchogenic carcinoma (52%) and bronchiectasis (67%). Studies with the reducing agent 2-mercaptoethanol (2-ME) suggested a role for IgM rheumatoid factor (RF) and/or IgM-containing complexes in the C1q-reactive material of sera from patients with bronchiectasis and bronchogenic carcinoma. In the latter two groups, C1qBA was found to correlate with serum levels of IgG and IgA but not with C3 and C4. A weak correlation between levels of C-reactive protein (CRP) and C1qBA was found in the bronchogenic carcinoma group. Carcinoembryonic antigen (CEA) levels were elevated in all groups studied but no correlation with C1qBA was demonstrated, suggesting that CEA or CEA-ICs, if present, do not have an influence on the C1qBA of such sera. The results indicate that elevated serum C1qBA is a concomitant of both chronic inflammatory and neoplastic diseases of the lung but the extent of any similarity in the non-immunoglobulin components of the immune complexes in the respective conditions remains unknown. (Author abstract) (28 Refs)

78. CERTAIN IMMUNOLOGIC ASPECTS OF PRIMARY NEOPLASMS OF THE LUNG (MEETING ABSTRACT).

Cengiarotti L, Mantovani G, Mathieu A, Brotzu G, Foddai G, Melis E, Piras SS, Pisano M, Fuxeddu G, Rosetti L, Vespa F, Del Giacco GS
Clinica Medica I, Universita di Cagliari, Cagliari, Italy
Tumori; 67(2,SupplA):220 1981

It has been known for sometime that patients with solid neoplasms had abnormalities in the number and function of their immunocompetent cells. Evaluation of these abnormalities has often been exploited for prognostic and therapeutic purposes. Hence within the limits of a chemo-immunotherapeutic protocol undertaken by our groups we have had an opportunity to study about 30 patients with primary lung neoplasms (non-small cell) with the following test: E rosette, active E rosette, rapid E rosette, T subpopulations, in vitro response to mitogens (phytohemagglutinin [PHA], concanavalin A [con A], pokeweed mitogen [PWM], membrane immunoglobulin analysis, carcinoembryonic antigen (CEA), beta-2-microglobulin, immune complexes and cutaneous responses to cross-reacting antigens. All of the patients were examined at the time of diagnosis and before any treatment including surgery. The most significant finding that emerged from our evaluation was that the majority (more than 75 per cent) showed a percentage and absolute drop in the number of T-lymphocytes. These barely respond to polyclonal mitogens. The skin tests also confirmed reduced operation of the delayed-type response. On the other hand the data were not consistent with respect to the percentage of active E rosettes and hence could not be evaluated very well. Whether the immunologic deficit precedes or is secondary to the neoplasm is not possible to determine at present. Nevertheless the increase in circulating immune complexes which could be detected with any frequency could suggest their interference with the cell-mediated response. The presence of cellular immunosuppression in subjects with primary neoplasms might suggest immunomodulating therapeutic measures. (no Refs) (In ITA)

79. EVALUATION OF CIRCULATING IMMUNE COMPLEXES IN 18 PATIENTS WITH OVARIAN TUMORS (MEETING ABSTRACT).

Benedetti Panici P, Di Roberto P, Sacco F, Margariti PA, Greggi S, Bellelli L, Sezzi ML
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Tumori; 67(2,SupplA):114 1981

Recent research conducted on neoplasm patients has revealed the presence of changes in humoral immunity such as the presence of circulating immune complexes which, according to some authors, seem to be identical to the 'blocking factors' responsible for the suppression of cellular immunity. We report preliminary findings from a pre- and postoperative evaluation of 18 patients not previously treated of whom 14 are International Federation of Gynecology and Obstetrics stage III and 4 stage IV. The immune complexes were determined by I125-labeled C1q complement fixation according to the method of Zuhler et al. Patients with cystadenocarcinoma had positive values (15 per cent compared to 100 per cent of the control represented by trichloracetic acid precipitate) in 16 cases out of 18 preoperatively, amounting to 88.8 per cent. Following surgery 2 cases became negative and for another 4 there was a non-significant reduction. It should be mentioned that 14 of the 18 patients had a 2 cm residual tumor following surgical excision. Currently there are studies in progress attempting to gather information on immune complex size and ability to bind to rheumatoid factor and conglutinin. (no Refs) (In ITA)

80. MEASUREMENTS OF CIRCULATING IMMUNE COMPLEXES IN CANCER PATIENTS (MEETING ABSTRACT).

Wilson RE, Rayner AA, Rodrick ML, Harte PJ, Munroe AE, Steele GD
Department of Surgery, Brigham and Women's Hospital, Boston, MA
Eur Surg Res; 13(1):32 1981

The presence of circulating immune complexes (CIC) has been demonstrated by numerous investigators using a variety of methods. We have modified the technique for aggregation of CIC by polyethylene glycol (PEG) which permits reproducible measurement by an increase in optical density and is not dependent on the class of immunoglobulin or the ability of the complexes to bind complement. Using this relatively simple test, we have critically analyzed the ability of this method to detect CIC using rabbit anti-BSA + BSA complexes. Soluble complexes were successfully detected in regions of antigen and antibody excess, and the results compared favorably with the classic Farr test for soluble complexes. We have compared the levels of CIC in normal human serum with those in the serum of patients with cancer and rheumatoid arthritis. In the cancer population, measurements have been made before and after surgical procedures - in patients with resectable or unresectable lesions - and in patients with or without sepsis. Patients with cancer had significantly higher PEG-CIC values than normals and lower values than rheumatoids. Patients with infection had significantly higher levels than normal while cancer patients with infection had significantly higher PEG-CIC levels than those with either cancer or infection alone. While mean preoperative values for patients with resectable and unresectable cancer were not different, PEG-CIC levels fell significantly in patients whose cancers were successfully resected. Patients with imcompletely resected malignancy showed no change in CIC levels in the postoperative sera. The possibility exists that levels of CIC in the serum can provide a record of biological events in cancer patients including tumor growth, response to treatment and cancer recurrence. (no Refs)

HUMORAL IMMUNOSUPPRESSIVE AGENTS

81. MEDICAMENTOUS IMMUNOSUPPRESSION IN DERMATOLOGY.

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Z Hautkr; 56(15):975-976,979-980,982-984,989-990 1981

The effect of immunosuppressive agents (glucocorticoid, azathioprine, methotrexate, cyclophosphamide, chlorambucile) on dermatologic diseases was studied in 102 patients. Complete cure was achieved in 9 patients, good improvement of the condition in 18 patients, moderate improvement in 21, and no effect in 19 patients. Among the 19 deceased patients, 4 had been suffering from dermatomyositis (a total of 13 dermatomyositis cases was treated). The relatively high rate of fatality in these cases was assumed to be due to paraneoplastic forms of the disease. The carcinogenic effect of cytotoxic substances had been studied earlier. Especially unfavorable is the combination of antigen stimulation and immunosuppression. Tumor risk is increased 50-100 fold if immunosuppressive therapy (IST) is administered after kidney transplantation. In 108 patients with autoimmune disease and IST, incidence of skin carcinoma was 24.1%, acute myeloid leukemia 25.9%, and lymphoma 19.5%. In 94 patients with autoimmune disease and no IST, the incidence rates were 9.5%, 3.2%, and 44.7%, respectively. (32 Refs) (In GER)

82. TUMOR ASSOCIATED IMMUNOSUPPRESSION IN MICE BEARING ANAPLASTIC CARCINOMA.

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Nuclear Medicine Service, Veterans Admin. Medical Center, Allen Park, MI, 48101

Immunol Commun; 10(1):45-58 1981

The effect of anaplastic carcinoma (15091A) and fibroblast cell culture supernates was examined in conjunction with concanavalin A on the splenic lymphocyte transformation of syngeneic A/J mice. Though both the tumor and normal cell culture supernates caused a dose-dependent suppression of the in vitro DNA synthesis of lymphocytes, larger depressive effects were observed with the former. Similar results were observed with supernates collected from tumor cell and fibroblast cultures in 10% heat inactivated fetal calf serum or serum-free media. The results of these experiments indicate that the depressed immunological reactivity observed in animals and humans with cancer may be attributed to enhanced release of immunosuppressive factor(s) by malignant tissue into the body fluids of hosts. (Author abstract) (43 Refs)

83. ANTI-BOVINE SERUM ALBUMIN (BSA) ANTIBODIES ARE A COMPONENT OF CIRCULATING IMMUNE COMPLEXES (IC) IN CHILDREN WITH NEUROBLASTOMA (NB) (MEETING ABSTRACT).

Beck DA, Rosen RD
University of Texas, M. D. Anderson Hospital Tumor Institute, Houston, TX
Pediatr Res; 15(4,Part2):573 1981

The Raji cell assay (RA) and C1q binding test (C1qBt) were used to monitor changes in IC levels over 1 to 15 mo in 17 patients with NB, 3 of whom were stage IVs. During the period of observation 19 tumor recurrences and 7 deaths were observed. IC were found in 10 of 62 samples (16.1%) by C1qBT and in 29 of 62 samples (46%) by RA. Changes in serum C1qBT or RA did not correlate with changes in disease activity or tumor burden. Sera from NB patients but not from age-matched controls precipitated a protein in 125I extrinsically labeled extracts of the LA-N1 NB cell line which had the mol wt and antigenic characteristics of BSA. Using a modified Farr assay, 11 of 17 patients had anti-BSA antibodies; 23% of the initial samples and 14% of the subsequent 61 sera contained more anti-BSA activity than was found in 95% of sera from 13 age-matched controls. Incubation at pH 3.0 overnight in the presence of 125I-BSA, followed by neutralization, substantially increased the anti-BSA activity of 3 sera with high levels of IC but did not influence the anti-BSA activity of 3 sera with moderate to low IC. This demonstration of abnormally increased anti-BSA activity as well as 'blocked' anti-BSA activity in IC suggests an altered reactivity to milk antigens or abnormal regulatory control of humoral immune responses in NB. (no Refs)

OTHER RELATED STUDIES

84. LY-M19: THE LYB-2 REGION OF MOUSE CHROMOSOME 4 CONTROLS A NEW SURFACE ALLOANTIGEN.

Tada N, Kimura S, Liu Y, Taylor BA, Hammerling Y
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Immunogenetics; 13(6):539-546 1981

Spleen cells from an SJL mouse immunized with 70Z/3 cells, an established pre-B cell line, were fused with cells of the nonsecretor myeloma line NS.1. One established hybridoma cell line (clone K10.6) continuously secreted antibody that recognized a new antigenic specificity tentatively named Ly-m19. This newly found antigen is detectable on both T and B cells. Cytotoxicity assays reveal that 75% of the spleen and lymph-node cells, 35% of bone marrow cells, and 15% of thymus cells reacted with antibody of clone K10.6. Strains expressing the specificity Ly-m19.1 are characterized by negative reactions and include the strains AKR, CE/J, RF/J, GR/A, SJL, P/J, BDP/J, and LG/J. All other strains so far tested are Ly-m19.2. This strain distribution pattern distinguishes Ly-m 19 from any known murine lymphocyte alloantigen, but it parallels the Lyb-2c haplotype. Linkage test of a set of AKXL recombinant inbred strains revealed close linkage of Ly-m19 and Lyb-2 loci on mouse chromosome 4. (Author abstract) (24 Refs)

85. A NEW MOUSE CELL-SURFACE ANTIGEN (LY-M18) DEFINED BY A MONOCLONAL ANTIBODY.

Kimura S, Tada N, Liu Y, Hammerling U
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Immunogenetics; 13(6):547-554 1981

Spleen cells from C3H/An mice immunized with spleen cells of C57BL/6-H-2k mice were fused with myeloma cell line NS.1. One established hybrid cell line continuously secreted antibody that recognized a new surface antigen provisionally called Ly-m18. The new alloantigen is expressed on 90% of thymus cells, 55% of spleen cells, and 45% of either lymph-node or bone-marrow cells. It is also expressed on cells derived from brain, kidney, and liver. Fifty percent of either peripheral T or B cells express the Ly-m18 antigen, and some tumor cell lines with T, B, pre-B or stem cell characteristics are Ly-m18 (+). The strain distribution pattern distinguishes Ly-m18 antigen from all other murine lymphocyte alloantigens. The typing data of two sets of CXB and AKXL recombinant inbred strains indicate that the Ly-m18 gene is linked to the Ltw-2 locus which has not yet been assigned to a chromosome. (Author abstract) (30 Refs)

86. SUPPRESSOR MONONUCLEAR CELLS IN GIANT LYMPH NODE HYPERPLASIA AND THYMOMA.

Shohat B, Cohen I, Fogel R, Zaizov R
Clinical Lab., Beilinson Medical Center, Petah Tikva, Israel
Cancer; 48(4):923-926 1981

The existence of suppressor mononuclear cells were demonstrated in two lymphoproliferative disorders: giant lymph node hyperplasia and thymoma. The three patients tested also showed cell-mediated immunodeficiency as expressed in the low number of T cells, negative graft vs host reactions and negative skin tests; the one patient tested with phytohemagglutinin (PHA) and concanavalin A (Con A) showed a low response. Suppressor activity was tested with a new experimental model, the local xenogeneic graft vs host reaction. It is proposed that this model be used for testing suppressor activities in other human disorders as well. (Author abstract) (14 Refs)

87. RAPID TURNOVER OF ARACHIDONYL-PHOSPHATIDYLINOSITOL IN L CELLS STIMULATED BY ANTIBODY.

Shearer WT, Richards JE
Dept. Pediatrics, Baylor Col. Medicine, Houston, TX, 77030
Biochem Biophys Res Commun; 101(3):800-806 1981

The incorporation of 14C-arachidonic acid into certain phospholipid fractions of antibody-stimulated mouse tumorigenic methylcholanthrene transformed (L) cell membranes was studied. Organic solvent cell extractions were separated by two-dimensional chromatography and counted for radioactivity by scintillation spectrometry. A clear dose-response relationship was found between IgG binding on and 32P incorporation into intact L cells; incorporation of 32P into an isolated phosphatidylinositol (PI) fraction of L cell membrane was increased by 56%. The degree of chromatographic separation of individual phospholipids indicated the relative rabbit L cell antibody-enhanced incorporation of 14C-arachidonic acid into the PI fraction (53% increase), a change which occurred without corresponding increase in 3H-glycerol incorporation. Two other isolated lipid fractions, phosphatidylcholine (PC) and phosphatidylethanolamine (PE), showed one half or less the PI 14C-arachidonic acid turnover enhancement. PI exhibited a 4.6

and 7.2 x more rapid turnover than PC and PE, respectively. The rapid incorporation of arachidonic acid into the PI membrane fraction may be an important initial event in the antibody-mediated immunological enhancement of tumor cell growth. (15 Refs)

88. EVIDENCE FOR INTERACTION BETWEEN T CELL POPULATIONS OF TUMOR-BEARING AND NORMAL MICE IN IMMUNE SUPPRESSION.

Iagenito GG, Calkins CE
Dept. Microbiology, Thomas Jefferson Univ., 1020 Locust St., Philadelphia, PA, 19107
J Immunol; 127(3):1236-1240 1981

Spleen cells of DBA/2 mice bearing sc implants of the syngeneic tumor L5178Y induce suppression of the in vitro antibody response of normal spleen cells to sheep RBC (SRBC). Cells mediating suppression are detected in the spleens of tumor-bearing mice as early as 24 hr post-implantation but are no longer detected there 15 days post-implantation. These spleen cells are nylon wool nonadherent, sensitive to anti-Thy 1.2 + C and anti-Lyt 1.1 + C, and insensitive to anti-Lyt 2.1 + C treatment. The anti-SRBC response of the unfractionated spleen cells from the tumor-bearing mice is not itself suppressed at the cell numbers used. This along with the finding that suppression occurs in the presence of spleen cells from normal mice suggest that a cell population from the normal mouse spleen is also involved in the suppression. Spleen cells from mice inoculated with irradiated (nonproliferating) L5178Y cells are similarly capable of mediating nonspecific suppression for the same limited period of time after the inoculation. In addition, spleen cells from mice stimulated with several nontumorigenic cellular antigens interact with normal spleen cells to produce suppression. These findings suggest that suppression observed in vitro with spleen cells from these tumor-bearing mice may be the result of antigen-activated cells triggering normal immunoregulatory cells. (Author abstract) (30 Refs)

89. MURINE T CELLS THAT LYSE ANTIBODY-SENSITIZED TARGET CELLS. III. CONTRIBUTION OF THY 1-BEARING CELLS TO THE LYTIC ACTIVITY OF NORMAL SPLEEN.

Lamon EW, Pollok BA, Walia AS, Fuson EW, Williams B
Univ. Alabama in Birmingham, Dept. Surgery and Microbiology, Birmingham Veterans Admin. Hosp., University Station, AL, 35294
Immunology; 43(4):643-651 1981

Murine spleen cells were analyzed for their capacity to lyse 51Cr-labeled antibody-sensitized RBC and a human lymphoma cell line. Incubation of spleen cells with iron powder followed by removal of iron-containing cells with a magnet significantly decreased the lytic capacity of the remaining cells against RBC target cells. However, substantial cytotoxicity remained in the relatively phagocyte-depleted population. Both antibody-sensitized RBC and tumor cells were lysed by phagocyte-depleted effector cells. However, more spleen cells were required to lyse nucleated target cells than were required to produce comparable lysis of the RBC. Such phagocyte-depleted spleen cells were subsequently treated with three different antisera containing specificities for thymus-dependent antigens and a monoclonal IgM anti-Thy 1.2 in the presence of complement. The remaining viable cells were recovered and tested as effector cells. All four reagents in the presence of complement caused an inhibition of antibody-dependent cell-mediated cytotoxicity (ADCC) that was proportional to the percentage of T cells eliminated. However, the antisera also inhibited ADCC in the absence of complement, even when the cells were trypsinized following the antiserum treatment to remove attached antibodies. On the other hand, treatment of spleen cells with the monoclonal IgM anti-Thy 1.2 followed by trypsin treatment did not inhibit ADCC unless complement was added. Thus, with the latter reagent, decreased ADCC could be ascribed to elimination of T cells and not immune complex inhibition. Cells bearing Thy 1.2 accounted for approx half of the lytic activity of phagocyte-depleted spleen cells against antibody-sensitized target cells. (Author abstract) (35 Refs)

90. MONOCLONAL ANTIBODY TO AFLATOXIN B1-MODIFIED DNA DETECTED BY ENZYME IMMUNOASSAY.

Haugen A, Groopman JD, Hsu IC, Goodrich GR, Wogan GN, Harris CC
Human Tissue Studies Section, Lab. Experimental Pathology, NCI, Bethesda, MD, 20205
Proc Natl Acad Sci USA; 78(7,part2):4124-4127 1981

Monoclonal antibodies were obtained after fusion of mouse P3 x 63 myeloma cells with spleen cells isolated from BALB/c mice that had been immunized with aflatoxin B1-adducted DNA complexed with methylated bovine serum albumin. Selected hybridomas were found to produce monoclonal antibodies specific for aflatoxin B1-modified DNA containing both the 2,3-dihydro-2-(N7-guanyl)-3-hydroxyaflatoxin B1 and the putative 2,3-dihydro-2-(N5-formyl-2',5',6'-triamino-4' oxo-N5-pyrimidyl)-3-hydroxyaflatoxin B1, suggesting that these DNA adducts share a common antigenic determinant. The monoclonal antibody was not reactive towards the free aflatoxin B1-guanine adducts in soln, seven other aflatoxin derivatives, or benzo[a]pyrene-adducted DNA. A noncompetitive ultrasensitive enzyme radioimmunoassay could measure 15 fmol of aflatoxin B1-DNA adducts in 10 ng of DNA and was at least 100-fold more sensitive than the standard enzyme-linked immunosorbent assay. Competitive enzyme-linked immunosorbent assay with these monoclonal antibodies reliably quantitated aflatoxin B1 adducted in vivo to rat liver DNA at adduct levels of one aflatoxin B1 residue per 250,000 nucleotides. The competitive ultrasensitive enzyme radioimmunoassay was determined to be at least 6-fold more sensitive than the competitive enzyme-linked immunosorbent assay in analysis of aflatoxin B1-adducted DNA. Therefore, enzyme immunoassay using monoclonal antibodies will be useful analytical tools for studying both the molecular interactions of aflatoxin B1 with DNA and the occurrence of aflatoxin B1-DNA adducts in biological specimens from people exposed to this environmental carcinogen. (Author abstract) (23 Refs)

91. THE EFFECT OF NEONATAL THYMECTOMY ON LUNG CANCERS INDUCED IN RATS BY PLUTONIUM DIOXIDE.

Nolibe D, Masse R, Lafuma J
Commissariat a l'Energie Atomique, Institut de Protection et de Surete, Nucleaire Laboratoire de Toxicologie Experimentale, BP 561, 92542 Montrouge Cedex, France
Radiat Res; 87(1):90-99 1981

A total of 258 three-mo old male and female Wistar rats were studied. Group I, 31 controls, were sham-thymectomized. Group II, 122 sham-thymectomized, were exposed to plutonium dioxide (PuO2) inhalation at the age of 90 days. Group III, 82 rats thymectomized within 24 hr of birth, were exposed to PuO2 inhalation at age 90 days. Radiation doses ranged from 100 to 1,500 rad. Group IV, 23 rats, were thymectomized only. Twelve rats from Group III and 5 from Group IV were lost due to infection or other reasons. The mean life span of thymectomized rats was significantly reduced compared to controls (588 vs 769 days). While thymectomy had no apparent effect on lung cancer incidence, it did lead to accelerated growth of spontaneous tumors a higher incidence of extrapulmonary tumors. In epithelial-type tumors of the lung, there was a shift from predominantly bronchioalveolar towards the bronchogenic type. The results indicate that immunosuppression should not affect the incidence of PuO2-induced lung cancer. It will, however, strongly affect the severity of development of cancer in potential carriers of the malignancy. (17 Refs)

92. MONOCLONAL ANTIBODY TO A NOVEL LYMPHOCYTE FUNCTION-ASSOCIATED ANTIGEN (LFA-1): MECHANISM OF BLOCKADE OF T LYMPHOCYTE-MEDIATED KILLING AND EFFECTS ON OTHER T AND B LYMPHOCYTE FUNCTIONS.

Davignon D, Marta E, Reynolds T, Kurzinger K, Springer TA
Lab. Membrane Immunochemistry, Sidney Farber Cancer Inst., Harvard Medical Sch., Boston, MA, 02115
J Immunol; 127(2):590-595 1981

The M7/14 monoclonal antibody (MAb) has previously been shown to block xenogeneic cytolytic T lymphocyte-(CTL) mediated killing by binding to the CTL rather than the target cell. It defines a novel surface antigen, termed LFA-1, with polypeptide chains of 180,000 and 95,000 Mr. The mechanism of this blockade and the effects of M7/14 on other T and B lymphocyte functional responses have been investigated here. Blockade of CTL-mediated killing is given by purified M7/14 MAb, and is not due to trivial mechanisms such as toxicity or agglutination. M7/14 blocks CTL directed to allogeneic and anti-modified self as well as xenogeneic determinants. Blockade occurs at the recognition-adhesion step, as shown by inhibition of CTL-target cell conjugate formation. M7/14 antibody was also shown to block a variety of other T cell functions: the mixed lymphocyte response (both in xenogeneic and allogeneic systems), antigen-specific T cell proliferation, and T cell-dependent plaque-forming cell responses, but not T cell-independent plaque-forming cell responses or LPS-induced B cell proliferation. Inhibition of both CTL and MLR function was extremely potent, occurring at MAb concentrations as low as 0.5 ug/ml. Inhibition of the MLR occurs in the 1st day of 6-day cultures. The data suggest that LFA-1 participates in or is closely associated with a number of different T lymphocyte functional pathways. LFA-1 appears crucial for the adhesive interaction between CTL and target cells, and it is possible that its importance in T helper and proliferative responses is also related to intercellular interactions. (Author abstract) (33 Refs)

93. A NOVEL LYMPHOCYTE FUNCTION-ASSOCIATED ANTIGEN (LFA-1: CELLULAR DISTRIBUTION, QUANTITATIVE EXPRESSION, AND STRUCTURE.

Kurzinger K, Reynolds T, Germain RN, Davignon D, Martz E, Springer TA
Lab. Membrane Immunochemistry, Sidney Farber Cancer Inst., Harvard Medical Sch., Boston, MA, 02115
J Immunol; 127(2):596-602 1981

We have previously described a monoclonal antibody (MAb), M7/14, which blocks a variety of T cell functions, including CTL-mediated killing, the mixed lymphocyte response, and antigen-specific proliferation. The antigen defined by M7/14 has been designated lymphocyte function-associated antigen one (LFA-1). In this report, LFA-1 has been studied as to cell distribution, surface abundance, structure, and in comparison to other CTL surface antigens. LFA-1 is expressed on lymphoid cells of both the T and the B lineages and on a large fraction of bone marrow cells, but not on exudate macrophages or non-lymphoid tissues. T cells express more LFA-1 than B cells, both in the unstimulated and stimulated states. Compared with unstimulated spleen cells, cytolytic T lymphocyte cell preparations (CTLP) and Con A blasts, but not LPS blasts, show increased LFA-1 expression relative to H-2, and for T cell-containing populations, Lyt-2. M7/14 MAb binds to about 1.5 x 10(4) LFA-1 sites per av spleen cell or CTLP cell, respectively. M7/14 MAb binds to CTLP in quantities of 2.5-fold and is 10.4-fold less than H-2 and Thy-1 MAb, respectively; since the latter have little or no effect on CTL function, inhibition of killing by M7/14 MAb is specific for the LFA-1 surface site. M7/14 MAb and a blocking Lyt-2 MAb are bound in similar quantities of CTLP. LFA-1 is a glycoprotein and consists of 2 noncovalently linked polypeptide chains of 180,000 and 95,000 Mr. The same molecular species as on CTL is present on other T cells and on B cells. The molecular structure and cell distribution of LFA-1 clearly distinguishes it from Lyt-2,3, Ly-5, T145, and T11, which were previously suggested to be either associated with the function of and/or present on the surface of CTL. (Author abstract) (42 Refs)

94. DIFFERENTIAL EFFECT OF INTERFERON ON THE EXPRESSION OF TUMOR-ASSOCIATED ANTIGENS AND HISTOCOMPATIBILITY ANTIGENS ON HUMAN MELANOMA CELLS: RELATIONSHIP TO SUSCEPTIBILITY TO IMMUNE LYSIS MEDIATED BY MONOCLONAL ANTIBODIES.

Imai K, Ng AK, Glassy MC, Ferrone F
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J Immunol; 127(2):505-509 1981

Incubation of cultured human melanoma cells with human leukocyte interferon did not change the expression melanoma-associated antigens (MAA) recognized by monoclonal antibodies and of Ia-like antigens but significantly increased the expression of HLA-A,B antigens and Beta2-microglobulin (B2-u). The effect is dependent on the dose of interferon and on the incubation time. Interferon-treated melanoma cells showed an increased susceptibility to lysis mediated by monoclonal antibodies to HLA-A,B antigens and to human B2-u; on the other hand, interferon-treated melanoma cells did not change in their susceptibility to murine natural (NK) cell lysis and to immune lysis mediated by monoclonal antibodies to MAA and to Ia-like antigens, and they displayed a reduced susceptibility to human NK cell lysis. Therefore, the increased susceptibility of interferon-treated melanoma cells to lysis mediated by anti HLA-A,B and anti B2-u monoclonal antibodies is likely to reflect the increase in cell surface expression of the corresponding antigens. (Author abstract) (29 Refs)

95. ANTIBODY RESPONSE TO PNEUMOCOCCAL VACCINE IN PATIENTS WITH MULTIPLE MYELOMA.

Schmid GP, Smith RP, Baltch AL, Hall CA, Schiffman G
(c/o Baltch) Infectious Disease Section, Veterans Admin. Medical Center, Albany, NY, 12208
J Infect Dis; 143(4):590-597 1981

Patients with multiple myeloma and Waldenstrom's macroglobulinemia respond poorly to antigenic stimuli and may not be protected by pneumococcal vaccine. Thirty-seven patients and 10 controls received 14-valent pneumococcal capsular polysaccharide vaccine. The patients had lower (p less than 0.01) titers of antibody to 11 of the 12 antigens assayed before vaccination and to 10 of 12 antigens (p less than 0.01) after vaccination than did controls, but the ratios of antibody titers before vaccination to those after vaccination were remarkably similar. A poorer antibody response was observed in patients receiving multiagent chemotherapy than in those receiving chemotherapy with alkylating agents (p less than 0.01 for 6 of the antigens). That these patients did respond to the vaccine (although titers of antibody after vaccination were significantly lower than those in controls) suggests that patients with multiple myeloma or macroglobulinemia may benefit from pneumococcal vaccine. (Author abstract) (28 Refs)

96. BURKITT'S TYPE ACUTE LYMPHOBLASTIC LEUKEMIA. CELLULAR PHENOTYPE AND CHROMOSOME ABNORMALITIES.

Demeocq F, Bernard A, Boumsell L, Bezou MJ, Turchini MF, Malpuech G

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Arch Fr Pediatr; 38(5):355-357 1981

The immunologic and cytogenetic analysis of a 13-yr old male patient with Burkitt's type acute lymphoblastic lymphoma is described. The lymphoblasts were found to carry IgS mu and gamma, with no IgD, and with only weak expression of the receptors for the constant fragment of IgG. This phenotype corresponded with a highly differentiated B cell line. A translocation between chromosomes 1 and 8 was observed. The implications of these findings are discussed. (12 Refs) (In FRE)

97. A SERUM-FREE MEDIUM FOR A431 HUMAN EPIDERMOID CARCINOMA CELLS; INHIBITION OF GROWTH IN CULTURE BY MOUSE EPIDERMAL GROWTH FACTOR (MEETING ABSTRACT).

Barnes D
Department of Biological Sciences, University of Pittsburgh, Pittsburgh, PA, 15260
63rd Annual Meeting of the Endocrine Society, June 17-19, 1981, Cincinnati, Ohio. The Endocrine Society 385 pp., 1981.

We have developed a serum-free medium which supports A431 growth as well as serum containing medium (SCM). The basic nutrient medium (BNM) was a 1:1 mixture of Ham's F12 and Dulbecco-modified Eagle's medium containing 1.2g/l NaHCO3 and 15 mM 4-(2-hydroxyethyl)-1-piperazine ethanesulfonic acid. To BNM were added 4 factors stimulatory for A431 cell growth (BNM4F): 10 ug/ml insulin, 10 ug/ml transferrin, 5 ug/ml cold-insoluble globulin (CIg) and 0.5 mM ethanolamine. Preincubation of culture dishes with 5 ug/ml CIg or serum spreading factor could substitute for addition of CIg directly to medium in which cells were plated. Cells plated at a density of 2.5X10(3)/cm2 in BNM4F grew with a doubling time (TD) of 30 hr; cell number after 6 days was 85-100% of that in plates with SCM. A small, reproducible increase in cell number was seen if BNM4F was further supplemented with 2 ug/ml glycyl-histidyl-lysine; small, inconsistent increases were sometimes seen upon addition of 5 ng/ml parathyroid hormone or 100 ng/ml somatostatin. A431 cells also grew in BNM, but at a reduced rate. Addition of EGF at concentrations mitogenic for other cell types caused marked inhibition of A431 growth. Inclusion of EGF in the medium also reduced plating efficiency and prolonged the time lag before onset of growth after plating; cell number after 6 days in culture in BNM4F with 100 ng/ml EGF was about 10% of cell number in BNM4F. Inhibitory effects of EGF were detectable at 1 ng/ml in BNM4F and also were seen in BNM and SCM. Cells exposed to 10 ng/ml EGF in BNM4F for 72 hr and changed to BNM4F without EGF resumed growth with TD near that of unexposed cell after a lag of about 72 hr. Decrease in cell number due to inclusion of 10 ng/ml EGF in BNM4F could be prevented partially by the simultaneous addition of 2.5 ug/ml rabbit anti-EGF antibody. A431 cells produced tumors in athymic mice of either sex. (no Refs)

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TUMOR ANTIBODY PRODUCTION/ CHARACTERIZATION/ DETECTION

1. THE USE OF LYMPHOCYTES FROM AXILLARY LYMPH NODES OF MASTECTOMY PATIENTS TO GENERATE HUMAN MONOCLONAL ANTIBODIES.

Wunderlich D, Teramoto YA, Alford C, Schlom J
(c/o Schlom) Lab. Cellular and Molecular Biology, NCI, NIH, Bethesda, MD, 20205
Eur J Cancer Clin Oncol; 17(7):719-730 1981

Lymphocytes from axillary lymph nodes of breast cancer mastectomy patients were fused with murine non-Ig-secreting

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myeloma cells to generate hybridoma cell lines that synthesize human Ig. Lymph node lymphocytes from 21 patients were used to obtain 505 human-mouse hybrid cultures. From these, 62 cultures were established which synthesized Ig reactive in radioimmunoassays specific for either IgG or human IgM. Some of these double-cloned hybrid cell lines produced human monoclonal antibodies for at least 6 mo. Sodium dodecylsulfate polyacrylamide gel electrophoresis and immunodiffusion analysis demonstrated that the monoclonal antibodies possessed human heavy and light Ig chains. Levels of synthesis ranged from 0.1 to 20 ug of human Ig per ml of culture fluid. The immunoreactivity of some of these human monoclonal antibodies with mammary carcinoma cells is summarized and has been documented elsewhere; the reactivity of the majority of the Ig, however, is still unknown at this time. The studies reported here detail the procedures in which axillary lymph nodes from mastectomy patients are used in the generation of human-mouse hybridomas that synthesize human monoclonal antibodies. (Author abstract) (14 Refs)

2. IN VITRO PRODUCTION OF HUMAN ANTIBODY TO A TUMOUR-ASSOCIATED FOETAL ANTIGEN.

Irie RF, Jones PC, Morton DL, Sidell N

Div. Oncology, Univ. California Sch. Medicine, 54-140 CHS, Los Angeles, CA, 90024

Br J Cancer; 44(2):262-266 1981

After the establishment of lymphoblastoid cell lines that synthesize antibody directed against a human tumor-associated fetal antigen designated as oncofetal antigen-I (OFA-I), a method is described for the production of IgM anti-OFA-I in vitro. Ten serum samples containing high levels of anti-OFA-I were identified and viably frozen peripheral-blood lymphocytes (PBL) from the same patients were transformed by Epstein-Barr virus (EBV). Patients included five given adjuvant immunotherapy with an OFA-I+ tumor-cell vaccine (TCV), three treated with BCG, and two treated only by surgical excision. Anti-OFA-I levels in the spent medium were monitored by immune-adherence using the OFA-I+ melanoma cell line UCLA-SO-M14 (M14), as the target cell. Two of the EBV-infected cultures (ES from the TCV group and CD from the surgery only group) produced detectable antibody to M14 cells by day 6. By day 9, culture DV (BCG group) became positive. The CD culture was positive only for 9 days, while ES (obtained from the patient with the highest anti-OFA-I titer) ceased growth after 3 wk. The supernatants displayed no reactivity against a control lymphoblastoid cell line autologous to the M14 donor. The DV lymphoblasts continued to produce increasing titers of anti-M-14 antibody until day 42, with gradual decrease by day 60 and became negative on day 66. None of the other 7 PBL cultures became positive to M14. Further studies determined that the antibody exhibited specific reactivity to an antigen associated with human cancer. No antibody reactivity in the DV culture medium was detected to a number of target cells tested. Assessment of the immunoglobulin class indicated the anti-OFA-I was limited to the IgM class. The DV spent medium was cytotoxic in the presence of either rabbit or human complement. (21 Refs)

3. A MONOCLONAL ANTIBODY DETECTING AN ANTIGEN SHARED BY NEURAL AND GRANULOCYTIC CELLS.

Kemshead JT, Bicknell D, Greaves MF

Membrane Immunology Lab., Imperial Cancer Res. Fund, Lincoln's Inn Fields, London, England

Pediatr Res; 15(9):1282-1286 1981

A monoclonal antibody, MI/N1, is described that reacts predominantly with fresh neuroblastoma tissue, human neuroblastoma cell lines, and cells of the myeloid lineage. Investigation of the binding of this antibody to four different neuroblastoma cell lines showed CHP 100 bound approx four times more antibody than CHP 126. Only 30% of the cells in the line CHP 100 bound MI/N1 as determined by indirect immunofluorescence. Thus, both quantitative and qualitative differences in the expression of antigen recognized by MI/N1 are detected on human neuroblastoma cell lines. Inasmuch as only five of eight marrow aspirates heavily infiltrated with neuroblasts bound the monoclonal, this also suggests a heterogeneity in antigenic expression on fresh tumor cells. Absorption studies indicate that the antigen recognized by MI/N1 is present on human fetal brain and adult human cerebellum. At a dilution of 1/750, equal vol of fetal brain and adult cerebellum absorbed out 30 and 60% of the reactivity to the human neuroblastoma cell line CHP 100. No reactivity was found towards murine neuroblastoma cells or rat brain. Expression of antigen on cells in the myeloid lineage appears dependent upon their stage of maturation, increasing as cells mature to neutrophils and eosinophils. It is suggested that the quantitative and qualitative differences seen in the expression of antigen on neuroblastoma cells may relate to their being blocked at different stages of differentiation. (Author abstract) (28 Refs)

4. DETECTION OF ANTIBODIES AND ANTIGENEMIA IN LEUKEMIC PATIENTS WITH CANDIDIASIS BY ENZYME-LINKED IMMUNOSORBENT ASSAY.

Meckstroth KL, Reiss E, Keller JW, Kaufman L

(c/o Reiss) Mycology Div., Centers for Disease Control, Atlanta, GA, 30333

J Infect Dis; 144(1):24-32 1981

Standard tests and two enzyme-linked immunosorbent assays (ELISAs) were compared for detecting systemic candidiasis in 92 leukemic patients. Antibodies to Candida were detected by immunodiffusion (ID), latex agglutination (LA), and indirect ELISA; antigenemia was evaluated by indirect ELISA inhibition. In 48 patients without candidiasis (Group 1), sera from 27% reacted in ID and 13% in LA tests; titers of antibody by ELISA occurred in all patients. In 34 patients without disseminated candidiasis (Groups 2 and 3), Candida species were isolated; sera from 35% and 32% were positive in the ID and the LA test, respectively. In 9 of 10 patients with disseminated candidiasis (Group 4), LA and ID tests were negati ve. Seven patients in Groups 1-3 without disseminated candidiasis were antigenemic (false-positive rate, 9%). Antigenemia was detected in 7 of 10 patients with disseminated candidiasis; in the remaining three patients sera were drawn too early to be of diagnostic value. Thus, monitoring of immunosuppressed patients for mannan antigenemia is useful for the detection of disseminated candidiasis. (Author abstract) (12 Refs)

5. ANALYSIS OF SERA FROM BREAST CANCER PATIENTS BY RADIOIMMUNOASSAYS.

Davis JW, Olive M, Cailleau R, Bowen JM
Dept. Molecular Carcinogenesis and Virology, Texas Medical Center, Univ. Texas System Cancer Center, MD Anderson Hosp. and Tumor Inst., Houston, TX, 77030
Cancer Immunol Immunother; 11(3):225-231 1981

Sera from 324 breast cancer patients were tested against various cell lines, including four human breast cancer, four human non-breast cancer, and three animal cell lines. Antibody reactivity was measured indirectly by binding antibodies to I125-labeled protein and directly using I125-labeled antibodies. Sera from 30 patients showed positive results, with nine different patterns of reactivity. Of these sera, two samples reacted positively only to human breast cell lines MDA-MB231 and MDA-MB330. Fifteen of the remaining 28 samples reacted with animal as well as human cell lines. Evidently breast cancer patients are sensitized to antigens occurring on breast cancer cells more often than normal individuals. Several different types of antigens, not all of which are specific to breast cancer cells, are detected by sera from such patients. The types of sera reactive only against breast cancer cell lines may be useful for the analysis of tumor-associated antigens. (36 Refs)

6. HUMAN TROPHOBLAST CELL-SURFACE ANTIGENS DEFINED BY MONOCLONAL ANTIBODIES.

Lipinski M, Parks DR, Rouse RV, Herzenberg LA
Laboratoire d'Immunologie Clinique, Institut Gustave-Roussy, 94800 Villejuif, France
Proc Natl Acad Sci USA; 78(8):5147-5150 1981

A series of monoclonal antibodies has been raised against the human choriocarcinoma cell-line, BeWo. Four antigens, Trop-1,-2,-3, and-4, are defined on normal and malignant trophoblast cells. Trop-1 and Trop-2 appear to be specifically expressed on syncytio- and cytotrophoblasts, whereas Trop-3 and Trop-4 are also detected on various tumor cell lines, normal lymphocytes, and monocytes. Anti-Trop-1 and and anti-Trop-2 antibodies might prove useful for detection and isolation of fetal trophoblast cells circulating in pregnant women's blood and for diagnosis and therapy in patients having choriocarcinomas and other germ-cell neoplasms. (Author abstract) (16 Refs)

7. CELL SURFACE ANTIGENS OF HUMAN RENAL CANCER DEFINED BY MOUSE MONOCLONAL ANTIBODIES: IDENTIFICATION OF TISSUE-SPECIFIC KIDNEY GLYCOPROTEINS.

Ueda R, Ogata S-I, Morrissey DM, Finstad CL, Szkudlarek J, Whitmore WF, Oettgen HF, Lloyd KO, Old LJ
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Proc Natl Acad Sci USA; 78(8):5122-5126 1981

Seventeen monoclonal antibodies derived from fusions with spleen cells of mice immunized with established culture lines of renal cancers identified 9 cell-surface antigenic systems. Six of the systems (gp160, S25, gp120r, gp120nr, gp115, and V1) represent antigens not previously described. the other three systems are related to HLA-A, -B, and -C heavy chain and A and B blood group antigens. The most restricted of the newly described antigens are gp160, S25, and gp120r. These determinants are found only on cells of renal origin, both normal and malignant, and represent differentiation antigens of human kidney. In addition to the difference in the mol wt of two of these antigens, gp160, S25, and gp120r can be distinguished on the basis of differential expression on a panel of cultured renal cancers and normal kidney epithelium and fetal kidney cells. Glycoproteins bearing gp120r share a determinant with renal gp120nr (as indicated by sequential precipitations with monoclonal antibodies that detect gp120r and gp120nr), but gp120nr is found on a broader range of cell types, including fibroblasts and cell lines derived from lung, bladder, and colon cancers. The two other new systems, gp115 and V1, have characteristics of broadly occurring differentiation antigens but can be distinguished from each other and from gp120nr by differences in mol wt, heat stability (V1 is a heat-stable determinant), and differential expression on cell types of diverse origin. (Author abstract) (9 Refs)

8. CELL HYBRIDIZATION: A MONOCLONAL MARKER AS A DIAGNOSTIC AID IN HEMATOLOGY AND ONCOLOGY.

Tilz GP, Beverley P, Becker H, Lanzer G, Sedlmayr P

Medizinische Universitatsklinik, Auenbruggerplatz 15, A-8036 Gratz, Austria

Acta Med Austriaca; 8(3):85-87 1981

A monoclonal marker for hematologic and oncologic purposes was developed. Male BALB/c mice were immunized sc with 4.5 x 10(6) human lymphocytes and boosted ip at monthly intervals with 2-5 x 10(6) of the same type cells. Four days after the last booster dose, spleen cells were obtained from the mice and fused with NS-1 plasmacytoma cells. Polyethylene glycol (40% soln) was used as a fusing agent. Cells were grown on selective heterophilic antibody titer medium. Cells were selected and cloned on the basis of antibody production. Clones were tested for antibody activity against infantile thymus, lymph node, tonsil, bone marrow, and various solid tumor tissues, as well as leukemic and erythroleukemic cells. One IgG 1-producing clone was identified that reacted with lymphoid cells, band cells, polymorphs, eosinophils, and macrophages. The clone did not react with erythropoietic cells or with undifferentiated carcinoma cells . It was designated H Le D 1. Use of this clone allows differential diagnosis of undifferentiated carcinomas and lymphoid malignancies. (10 Refs) (In GER)

9. SPECIFICITY OF A MONOCLONAL ANTI-K 562 ANTIBODY.

Schienle HW, Muller-Ruchholtz W

Dept. Immunology, Univ. Kiel, Brunswiker Strasse 2-6, D-2300 Kiel, W. Germany

J Cancer Res Clin Oncol; 101(1):109-110 1981

Clone cells secreting an IgG antibody were obtained by immunizing female BALB/c mice with normal bone marrow cells and then hybridizing the mouse spleen cells with myeloma cells. The monoclonal antibody reacted preferentially with the K 562 cell line established from the pleural exudate of a patient in chronic myelocytic leukemia blast crisis. Weekly positive reactions were seen with a B-cell line (Daudi) and a monocyte cell line (U 937). The antibody, therefore, appears to define an antigen present on pluripotent stem cells in a high concentration and on slightly more differentiated precursor cells in a low concentration. (7 Refs)

10. LOCALIZATION OF MAMMARY TUMORS IN VIVO WITH 131I-LABELED FAB FRAGMENTS OF ANTIBODIES AGAINST MOUSE MAMMARY EPITHELIAL (MME) ANTIGENS.

Wilbanks T, Peterson JA, Miller S, Kaufman L, Ortendahl D, Ceriani RL
(c/o Peterson) Bruce Lyon Memorial Res. Lab., Children's Hosp. Medical Center, 51st and Grove St., Oakland, CA, 94609
Cancer; 48(8):1768-1775 1981

The Fab fragments of antibodies against cell-type-specific surface antigens of mouse mammary epithelial cells (MME-antigens) were used to localize mammary tumors successfully. The radioiodine-labeled anti-MME (Fab) was injected into mice carrying simulated mammary metastases, and after 24 hr the amounts of label per gram of excised tissue was several times greater in the tumor than in liver, brain, lung, or muscle. Kidney showed considerable accumulation of label but this appeared to be nonspecific. Kinetic studies revealed a rapid elimination of labeled Fab in the urine with only 1% of the injected dose remaining in the entire blood pool after 24 hr. With a high-purity germanium camera, mammary tumors were clearly located by the 131I-labeled anti-MME (Fab), and normalization to 99mTc-pertechnetate distribution in the animal increased the specificity. The density of 131I-label was fourfold greater over the mammary tumor than over comparable areas of the mouse. No accumulation of 131I-anti-MME (Fab) was observed in nonmammary tumors nor in mammary tumors when labeled nonspecific Fab was used. An analogous system using an anti-human mammary epithelial antiserum is being developed for localization of breast metastases in humans. (Author abstract) (40 Refs)

11. SYNGENEIC IMMUNE RESPONSE TO RAT TRACHEAL EPITHELIAL CELLS TRANSFORMED IN VITRO BY N-METHYL-N-NITRO-N-NITROSOGUANIDINE.

Braslawsky GR, Steele V, Kennel SJ, Nettesheim P
Biology Div., Oak Ridge Natl. Lab., Oak Ridge, TN, 37830
Br J Cancer; 44(2):247-257 1981

Two cell lines (2-10-1 and 8-10-2) derived by exposure of primary tracheal explants to MNNG in vitro were not tumorigenic in syngeneic F-334 rats or athymic BALB/c (nu/nu) mice at early passage, but became tumorigenic at late passage. These cell lines are therefore suited to study the expression of neoantigens during neoplastic development. Transplantation resistance to late-passage, tumorigenic cells was induced in syngeneic rats using an immunization protocol of repeated cell inoculation and tumor ablation. Spleen cells from such animals were reactive in 20h microcytotoxicity assays against neoplastic cell lines, but unreactive to normal tracheal epithelial cells. Similarly, immune spleen cells co-cultivated in vitro for 6 days with irradiated neoplastic cell lines before assay for microcytotoxicity were strongly reactive, whereas co-cultivation with normal epithelial cells did not stimulate reactivity. Antibody to these neoplastic cell lines was demonstrated in sera of tumor-resistant rats by an indirect radiolabeled-antibody binding test and by indirect immunofluorescence. There was no significant binding to normal tracheal epithelial cell outgrowths. (Author abstract) (28 Refs)

12. MONOCLONAL ANTIBODIES SPECIFIC FOR SIMIAN VIRUS 40 TUMOR ANTIGENS.

Harlow E, Crawford LV, Pim DC, Williamson NM
Dept. Molecular Virology, Imperial Cancer Res. Fund Lab., London WC2A 3PX, England
J Virol; 39(3):861-869 1981

Thirty hybridomas that secrete Ig against the simian virus 40 tumor antigens were isolated and cloned. Of these, 28 produced antibodies which bound to simian virus 40 large-T, and 2 produced antibodies which bound to the host 53,000-dalton protein. As in previous work, large-T antigen was found to have at least one determinant that it shared with small-t antigen and to have a minimum of six unique determinants. Several of the monoclonal antibodies from the L series hybridomas recognized determinants that were present on a subset of the large-T antigen from simian virus 40-transformed mouse cells. These monoclonal antibodies should be useful in studies of the structure and function of the simian virus 40 tumor antigens. (Author abstract) (30 Refs)

TUMOR ANTIBODIES ASSOCIATED WITH VIRUSES

13. G(ERLD): A CELL SURFACE ANTIGEN OF THE MOUSE RELATED TO XENOTROPIC MULV DEFINED BY NATURALLY OCCURRING ANTIBODY AND MONOCLONAL ANTIBODY. RELATION GIX, G(RADA1), G(AKSL2) SYSTEMS OF MULV-RELATED ANTIGENS.

Obata Y, Stockert E, DeLeo AB, O'Donnell PV, Snyder HW, Old LJ
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
J Exp Med; 154(3):659-675 1981

G(ERLD), one of the gp70-related cell surface antigens of murine leukemia virus (MuLV), is described and its features compared with the characteristics of other gp-70-related cell surface antigens, GIX, G(RADA1), and G(AKSL2). Sera from hybrid mice of crosses between B6 and 129, and their GIX congenic partners, B6-GIX+ and 129-GIX-, were tested for naturally occuring cytotoxic antibodies against a panel of transplanted tumor lines. Some sera were found to have high cytotoxic activity against ERLD, an x-ray-induced leukemia of B6 origin, as well as against other tumors. The G(ERLD) specificity was identified. The strain distribution of G(ERLD) was distinct from any known cell surface antigens. Quantitative differences in G(ERLD) expression characterized G(ERLD)+ strains. Most GIX+ strains were G(ERLD)+, while most GIX- negative strains were G(ERLD)-. Hybrids between G(ERLD)+ and G(ERLD)- strains expressed approx half the quantity of G(ERLD) found in the G(ERLD)+ parent. G(ERLD) was expressed in G(ERLD)+ mouse strains and in some G(ERLD)- strains. G(ERLD) could be expressed on tumor cells in the absence of other MuLV antigens. The occurrence of natural antibody with high ERLD reactivity was restricted to B6, B6-GIX+, C57L, and hybrid mice of crosses between B6, 129, and GIX congenic partner strains. Experimental results suggested that G(ERLD) expression was controlled by a single locus in B6, by two unlinked loci in 129 and by three unlinked loci in B6-GIX+ mice. It was suggested that one of the loci in 129 and B6-GIX+ mice may be identical or closely linked to the locus controlling GIX antigen expression. Evidence suggested that G(ERLD) is a determinant associated with xenotropic and dualtropic MuLV gp70 molecules, but that it is unstable and tends to be lost during standard purification procedures. A monoclonal antibody to G(ERLD) was produced. (37 Refs)

14. CORRELATION BETWEEN THE PRESENCE OF NATURAL ANTITUMOR ANTIBODIES AND ACTIVATION OF MULV ENDOGENOUS VIRUS IN BALB/C MICE.

Menard S, Colnaghi MI, Tagliabue E
Istituto Nazionale Tumori, Via G. Venezian 1, 20133 Milano, Italia
Tumori; 67(4):283-292 1981

Individual 3-mo-old or 12-mo-old BALB/c mice, as well as 5-mo-old nu/nu or nu/+ BALB/c mice, showed a direct correlation between the serum level of natural antitumor cytotoxic antibodies and the capacity of spleen cells to infect SC-1 cells permissive for murine ecotropic viruses. Pooled or individual sera from 3-mo-old BALB/c mice, negative for the presence of natural antitumor cytotoxic antibodies and whose spleen cells were unable to infect the SC-1 cells, were negative both for SC-1 cells and SC-1 cells infected by MuLV. On the contrary, pooled or individual sera from 15-mo-old BALB/c mice, positive for the presence of natural antitumor antibodies and with infecting spleen cells, were cytotoxic for infected SC-1 cells but not for the uninfected ones. The infection of SC-1 cells by MuLV could be inhibited by 3-mo- old spleen cells, and this effect was suppressed by depriving the inhibiting spleen cells of T cells by means of an anti-Thy-1 antibody plus complement. The cells with infectious capacity did not belong to the T-cell compartment, as demonstrated by the lack of infection after passing the infecting spleen cells through an anti-Ig column, whereas T-deprivation did not modify the infectious capacity. A natural anti-gp 70 monoclonal antibody, which exerted a complement-dependent cytotoxic effect on tumor cells, strongly inhibited the infection of the permissive SC-1 cells by MuLV. (Author abstract) (24 Refs)

15. IMMUNOPATHOLOGY OF NATURAL AND EXPERIMENTAL LYMPHOMAS INDUCED BY WILD MOUSE LEUKEMIA VIRUS.

Bryant ML, Scott JL, Pal BK, Estes JD, Gardner MB
(c/o Gardner) Dept. Pathology, Univ. California Sch. Medicine, Davis, CA, 95616
Am J Pathol; 104(3):272-282 1981

Naturally occurring lymphomas of Lake Casitas (LC) wild mice, and the lymphomas induced by LC murine leukemia virus (MuLV) in Swiss mice from the National Institutes of Health, displayed remarkably similar gross, microscopic, and functional characteristics. They spared the thymus, arose primarily in the splenic red pulp, became leukemic, and were comprised of stem cells lacking classic T- and B-cell markers. Cytoplasmic and surface Ig were undetectable in 34 of 35 spontaneous LC lymphomas and in any of 10 LC MuLV-induced lymphomas in NIH Swiss mice. Assays for Ig secretion, complement (C'3) and Fc receptors, Thy 1.1,2 antigens, Ly 1,2 antigens, and erythroid and myeloid markers were negative on all of the spontaneous and experimental lymphomas. Cell lines were derived from five spontaneous lymphomas of LC mice. Three lines were characterized as null cells, one line as B cells, and one line as macrophages. All cell lines were diploid. The wild mouse spontaneous lymphomas, and lymphomas experimentally induced by LC MuLV in laboratory mice, provide a useful model for childhood acute lymphoblastic leukemia and for study of the early steps of B-lymphocyte differentiation. (Author abstract) (64 Refs)

16. ANALYSIS OF THE NONVIRAL ANTIGENS IMMUNOPRECIPITABLE BY SV40 T ANTIBODY FROM SV40-TRANSFORMED HUMAN/MOUSE HYBRID CELL LINES.

Stitt DT, Mangel WF
(c/o Mangel) Dept. Biochemistry, Univ. Illinois, Urbana, IL, 61801
Virology; 114(1):149-160 1981

The expression of nonviral antigens, ie, host-coded proteins with mol wt from 48,000-56,000 (48K-56K) immunoprecipitable from extracts of simian virus 40 (SV40)-infected or -transformed cells by anti-SV40 tumor antibody, was examined in four SV40-transformed human cell lines, one SV40-transformed mouse cell line, and eight SV40-transformed human/mouse somatic cell hybrid cell lines produced by fusion of SV40-transformed human cells with untransformed mouse cells. Differences were found in the patterns of expression of these viral induced proteins among the human cell lines, between the human and the mouse cell lines, and between the human/mouse somatic cell hybrid cell lines and the human lines from which they were derived. Two of the human cell lines expressed only a 55K nonviral antigen; two expressed both a 55K and a 52K nonviral antigen. The mouse cell line expressed both a 55K and a 48K nonviral antigen. Each hybrid cell line expressed a 55K and also a 48K nonviral antigen, except one. The BALB IV-8 hybrid cell line expressed 55K and 52K nonviral antigens. By comparing the tryptic peptides fractionated on cation exchange columns of the nonviral antigens we determined: (1) the 48K nonviral antigen in human/mouse hybrids is encoded by a mouse chromosome. (2) The 52K nonviral antigen in the BALB IV-8 human/mouse hybrid is encoded by a mouse chromosome. It is possibly a precursor to the mouse 48K protein because it contains one extra tryptic peptide in addition to those of the mouse 48K protein, because one peptide has an altered mobility and because the 52K protein is found, so far, only in a human/mouse hybrid that does not exhibit a 48K nonviral antigen. (3) The 55K nonviral antigen in the C57-VII-6 human/mouse hybrid is encoded by a human chromosome. In the BALB IV-8 human/mouse hybrid, there is a 55K protein encoded by a human chromosome and probably a 55K protein encoded by a mouse chromosome. (4) If the gene encoding the human 55K nonviral antigen is located on a single chromosome, it is located on human chromosome 7. (Author abstract) (25 Refs)

17. NEW CELL SURFACE GP70 RELATED TO FRIEND MINK CELL FOCUS-INDUCING VIRUS IS EXPRESSED ON FRIEND VIRUS-INDUCED ERYTHROLEUKEMIC SPLEEN CELLS AFTER ELIMINATION OF ECOTROPIC FRIEND VIRUS GP70 IN RFV-3R/S MICE.

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J Exp Med; 154(3):868-882 1981

The expression of individual Friend virus (FV)-encoded proteins in FV leukemic spleen cells was studied at various times in the course of FV leukemia in order to determine the role of anti-FV antibody in altering the expression of viral antigens and infectious virus release in these cells. The results indicated that the presence of anti-FV antibody late in the disease is associated with a decreased expression of Friend helper virus (FMuLV)-encoded intracellular and cell surface proteins, whereas the expression of the replication-defective spleen focus-forming virus (SFFV)-encoded proteins appears to be minimally altered. This selective loss of F-MuLV proteins appeared to correlate with the specificity of the mouse anti-FV antibody that was found to recognize F-MuLV but not SFFV-specific proteins. In addition, a new gp70 molecule was identified on the surface of FV leukemic spleen cells late in the disease. This molecule differed from gp70 in the ecotropic Friend virus, which was inoculated into these mice, in that it shares cross-reactivity with Friend mink cell focus-inducing virus. The potential importance of this recombinant is discussed. (32 Refs)

18. IMMUNOPREVENTION OF FRIEND VIRUS-INDUCED ERYTHROLEUKEMIA BY VACCINATION WITH VIRAL ENVELOPE GLYCOPROTEIN COMPLEXES.

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Virology; 113(2):602-612 1981

Adult STU mice were repeatedly immunized with aggregates of Friend virus envelope glycoprotein gp85. The antigen was given emulsified in incomplete Freund's adjuvant. After the last boost, animals were challenged with a dose of FLV inducing fatal erythroleukemia in 90-100% of the controls. Twenty of 20 mice immunized with 100 ug of gp85 were completely protected, while 3 of 7 animals vaccinated with 10 ug of gp85 died of leukemia. Smaller doses were ineffective, as was the adjuvant alone. Only animals that had developed a strong antibody response survived the FLV challenge. Serum antibodies of these animals reacted with type-, species-, and interspecies-specific determinants of pg85. Only a marginal cellular reactivity to gp85 was detected. The development of viremia was monitored by the use of radioimmunoassay for the internal viral core polypeptide p30. Animals completely protected were not viremic later than 7 days post-FLV infection. Those mice of the immunized groups which died in spite of an early antibody response showed a sharp decrease in serum antibodies to gp85 and a simultaneous appearance of virus in blood about 2-4 wk before death from leukemia. Thus, the suppression of virus spread by antibody seems to be important for immuno-prevention of this virus-induced leukemia. (Author abstract) (26 Refs)

19. HATCHERY-RELATED CONTACT TRANSMISSION AND SHORT-TERM SMALL-GROUP-REARING AS RELATED TO LYMPHOID-LEUKOSIS-VIRUS-ERADICATION PROGRAMS.

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Avian Dis; 25(3):667-677 1981

Pathogen-free chickens of a cross highly susceptible to lymphoid leukosis virus (LLV) were examined to determine (1) the rate of transmission of LLV from congenitally infected chicks to uninfected chicks in the hatcher and the concomitant effect of manual vent sexing on this transmission, (2) the rate of contact transmission of LLV in chickens reared on a wire-mesh floor compared with that in chickens reared on a solid floor, and (3) the efficiency of short-term small-group-rearing in brooding battery and colony cages in preventing LLV transmission from infected to uninfected groups of chicks. In the first experiment, susceptible chicks exposed only in the hatcher were not LLV infected when tested for virus and antibody at 16 wk; however, 37/39 susceptible chicks exposed at hatching and then manually vent-sexed on the day of hatch and then reared in isolation had LLV-neutralizing antibody in their sera, and the rate of transmission varied directly with the length of time that contact exposure continued after hatching. In the second experiment, rearing chickens on a solid floor enhanced the rate of contact transmission of LLV; when examined at 16 wk, chickens raised on the wire-mesh floor had a lower incidence of infection (p less than 0.01) than those reared on the solid floor. In the third experiment, the indirect contact between infected and uninfected susceptible chicks did not result in transmission of LLV. These results indicate that intimate direct contact is necessary for the rapid transmission of LLV from infected to uninfected chicks. (25 Refs)

20. DEMONSTRATION OF AVIAN SARCOMA VIRUS-CODED PP60SRC IN VIVO AND THE ANTI-PP60SRC IMMUNE RESPONSE IN CHICKENS.

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J Virol; 39(3):950-953 1981

The avian sarcoma virus (ASV)-coded transforming protein pp60src was originally detected in vitro in ASV-transformed avian and mammalian cells in experiments involving mammalian antisera to ASV-induced tumors. It is demonstrated here that pp60src is also expressed in vivo in ASV tumors of chickens. Furthermore, the existence of the endogenous pp60src in all chicken cells does not impair the immune response to exogenous pp60src in the chicken. Whereas chicken antibodies can bind to pp60src, they do not serve as substrates for the protein kinase activity of this transforming protein. (Author abstract) (8 Refs)

21. ANTIBODIES SPECIFIC FOR THE POLYOMA VIRUS MIDDLE-SIZE TUMOR ANTIGEN.

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Proc Natl Acad Sci USA; 78(8):4882-4886 1981

We have obtained antibodies specific for the polyoma virus middle-size tumor antigen (middle T antigen) by immunizing rabbits with a synthetic peptide, Lys-Arg-Ser-Arg-His-Phe, corresponding to the six carboxy-terminal amino acids of the middle T antigen predicted from the nucleotide sequence of polyoma DNA. The antipeptide serum precipitates the polyoma middle T antigen but not the small or large tumor antigens, and precipitation is inhibited in the presence of the peptide. Two cellular proteins, 30,000 and 26,000 daltons, are also precipitated specifically by the antipeptide serum and may have amino acid sequences related to the peptide. Two other cellular proteins, 33,000 and 25,000 daltons, are precipitated only in the presence of the peptide and may associate with it in cell extracts. Antisera directed against synthetic peptides are likely to be important in various ways, including the production of antibodies directed against particular determinants and the recognition of unknown proteins whose genes have been analyzed. (Author abstract) (21 Refs)

22. ASSOCIATION OF EPSTEIN-BARR VIRUS WITH NASOPHARYNGEAL CARCINOMA IN ALASKAN NATIVE PATIENTS: SERUM ANTIBODIES AND TISSUE EBNA AND DNA.

Lanier AP, Bornkamm GW, Henle W, Henle G, Bender TR, Talbot ML, Dohan PH
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Int J Cancer; 28(3):301-305 1981

Biopsy specimens from Alaskan Native patients with nasopharyngeal carcinoma (NPC) and from other patients seen on the otolaryngology service were tested for Epstein-Barr virus-specific DNA and nuclear antigen (EBNA). Serum samples from both groups were tested for various EBV-related antibodies. EBV DNA and EBNA results were in agreement in 29 of 31 tissue specimens tested by the two methods. Ten of 11 biopsies containing NPC cells were positive for EBV DNA. Two NPC patients had biopsies that showed only atypical epithelium but were also positive for EBV DNA or EBNA. The other tissue specimens were negative except for biopsies from two patients: one with a parotid gland lymphoepithelial lesion; another with undifferentiated carcinoma of salivary gland origin. (Author abstract) (28 Refs)

23. EPSTEIN-BARR VIRUS INFECTION AND NEOPLASIA.

Sprinkle PM, Veltri RW
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Otolaryngol Head Neck Surg; 89(4):542-544 1981

Conclusive serological data of activation of Epstein-Barr virus (EBV) is reported showing persistently elevated early antigen (EA) titers prior to and following malignant transformation in a 6-yr-old boy. Heterophil-negative EBV disease characterized by lymphadenopathy and recurrent tonsillitis developed in the child 1 mo after his sister died with heterophil-negative infectious mononucleosis. Epstein-Barr nuclear antigen (EBNA) and EA were detected in many B-lymphocytes present in each of the same tissue specimens. One yr later, rebiopsy of the cervical nodes revealed typical Hodgkin's disease. EBNA and EA were found in hilar and celiac lymph nodes as well as in splenic lymphocytes. Serum antibody study demonstrated a 1:640 EA and 1:2,560 viral capsid antigen-IgG specific antibody to their EBV-coded antigens. Before and after the diagnosis of Hodgkin's disease, however, the patient's EA titers were persistently elevated and remained so. The child was alive with a poor prognosis after multiple chemotherapy courses and two courses of radiotherapy. The child's mother died in the interim with undifferentiated lymphoma. (16 Refs)

ANTITUMOR ACTIVITY AND IMMUNOTHERAPY

24. EXPRESSION OF COMMON ACUTE LYMPHOBLASTIC LEUKEMIA ANTIGEN (CALLA) BY LYMPHOMAS OF B-CELL AND T-CELL LINEAGE.

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Blood; 58(3):648-652 1981

Previous studies have demonstrated that the common acute lymphoblastic leukemia antigen (CALLA) is expressed by leukemic cells from approx 80% of patients with non-T-cell ALL and 30%-50% of patients with chronic myelocytic leukemia in blast crisis. A small number of normal bone marrow and fetal liver cells also express CALLA, but the functional role of this molecule is unknown. In the present study, we have used a monoclonal antibody (J5) specific for CALLA to study the expression of this antigen in non-Hodgkin's lymphomas. Within the B-cell lymphomas, it was found that CALLA was expressed by almost all Burkitt's and nodular poorly differentiated lymphocytic lymphomas. Within the T-cell lymphomas, CALLA was expressed in 40% of patients with lymphoblastic lymphoma. Three of three Burkitt's lymphoma cell lines and three of eight T-lymphoblast cell lines were also found to express CALLA. Normal spleen, lymph node, and thymus cells were not reactive with J5 antibody. These findings indicate that expression of CALLA is not limited to relatively undifferentiated leukemic lymphoblasts but also occurs in more differentiated lymphoid malignancies. However, normal differentiated lymphoid cells in lymph node, spleen, and thymus, which have a phenotype similar to that of lymphoma cells, do not appear to express CALLA. (Author abstract) (26 Refs)

25. SURFACE PHENOTYPE OF JAPANESE ADULT T-CELL LEUKEMIA CELLS CHARACTERIZED BY MONOCLONAL ANTIBODIES.

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Blood; 58(3):645-647 1981

We studied the surface phenotype and the functional activities of leukemic cells from three patients with Japanese adult T-cell leukemia (ATL) using the panel of OK and anti-Tac monoclonal antibodies, which react with differentiation antigens and define functionally distinct T-cell subsets or activated and terminally differentiated to T cells. The phenotype of ATL cells were determined to be OKT1+T3+T4+T10+T5-T8-OKIa1-, although cells from two patients suppressed pokeweed mitogen (PWM) induced normal B-cell differentiation, and cells from all patients lacked helper activity in this system. In addition, after cultivation with PWM, ATL cells from all patients were reactive with anti-Tac monoclonal antibody, and cells from one patient were reactive with OKIa1. These findings suggest that ATL cells arise from peripheral mature T-cell subsets and also suggest that the transition of surface phenotype of ATL cells to functionally mature and activated T cells occurs in culture. (Author abstract) (17 Refs)

26. DISTRIBUTION AND MOLECULAR CHARACTERIZATION OF A CELL-SURFACE AND A CYTOPLASMIC ANTIGEN DETECTABLE IN HUMAN MELANOMA CELLS WITH MONOCLONAL ANTIBODIES.

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Int J Cancer; 28(3):293-300 1981

The monoclonal antibodies 225.28S and 465.12 to human melanoma-associated antigens have been tested with a large variety of surgically removed skin lesions and malignant tumors as well as with a panel of cultured cell lines in serological and immunochemical assays. The antibody 225.28S reacts with a plasma membrane antigen while the antibody 465.12 detects a cytoplasmic antigen. Both antibodies fail to react with melanocytes from normal skin as well as benign skin lesions but react with nevi, melanoma cells and some skin carcinomas. Analysis with surgically removed tumors and cultured human cell lines indicated that the plasma membrane antigen is restricted to skin lesions whereas the cytoplasmic antigen is synthesized by tumor cells of various histological origins. The plasma membrane antigen is composed of two glyco-polypeptides of 280,000 and greater than 440,000 daltons, while the cytoplasmic antigen consists of four glycopolypeptides of 94,000, 75,000, 70,000 and 25,000 daltons. None of these components are bridged by disulfide bonds. The cytoplasmic antigen was readily detected in the spent culture medium of melanoma cell lines in the form of a major 94,000 dalton and a minor 72,000 dalton structure, while the plasma membrane antigen was detectable only after vastly increasing the sensitivity of the assay system. (Author abstract) (23 Refs)

27. QUANTITATIVE IMMUNOFLUORESCENT ANALYSIS OF SURFACE PHENOTYPES OF MURINE B CELL LYMPHOMAS AND PLASMACYTOMAS WITH MONOCLONAL ANTIBODIES.

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Immunology Lab., Dept. Pathology and Medicine, Univ. New Mexico Sch. Mediçine, Albuquerque, NM, 87131
J Immunol; 127(4):1691-1697 1981

In this study, a large series of murine B lymphomas and plasmacytomas were examined by quantitative flow cytometry analysis using a panel of monoclonal antibodies against murine differentiation antigens. These cell lines appear to represent subpopulations of lymphoid cells arrested at distinct stages of differentiation. In general, the pattern of reactions of these monoclonal antibodies with the B cell neoplasms was comparable to the reactions seen with normal cells in the same lineage. The Thy-1.2, Lyt-2, and T-30 differentiation antigens were not detected on any B lymphoma or plasmacytoma. However, certain surface Ig-positive B lymphomas do express the Lyt-1 antigen. With respect to other differentiation markers examined, including E2, F1, ThB, Lgp-100 (Ly 9.1), G2, and T-200 (Ly 5), the reaction of the B cell tumors reflected the expression of these markers on comparable normal cells. This investigation also emphasized the marked intratumor and intertumor heterogeneity that is observed when cloned cell lines are analyzed quantitatively for a large number of surface markers. Thus, this approach may be particularly useful in defining heterogeneity in maturation states within cloned tumor cell lines. (Author abstract) (33 Refs)

28. IMMUNOFLUORESCENCE OF ORAL SWABS- A NEW METHOD FOR EARLY RECOGNITION OF RECURRENCES OF TONSILLARY CARCINOMA?.

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Laryngol Rhinol Otol (Stuttg); 60(7):385-386 1981

Immunofluorescent method for the early detection of recurrence of tonsillar carcinoma and its application in 54 patients are reported. Sera of patients with squamous-cell carcinoma of the tonsil contain antibodies of IgG type, which seem to be directed against individual-specific and group-specific tumor cell surface antigens. Such antibodies, which react with antigen on tumor cells from surgical specimens, also label presumably malignant cells from oral swabs. The immunofluorescent test, performed on 67 oral swabs from 54 patients, was positive in 7% of the patients in good condition, in 17% of those in poor condition, and in 88% of those with recurrence. The test result was uncertain in 17% of the patients in good condition, 59% of those in poor condition, and in 12% of the patients with recurrence. The test results were positive in 76% of the patients in good position, in 27% of those in poor condition, and in 0% of the patients with recurrence. Fluorescence was found in nine patients without clinical and histological evidence of recurrence 0.5-1.5 yr after the completion of therapy. Eight of these nine patients developed clinically and histologically confirmed recurrence within 1 yr, mostly within 3-6 mo, after the immunofluorescence test. The findings indicate the prognostic and diagnostic value of this simple non-invasive method in patients with tonsillar carcinoma. (9 Refs) (In GER)

29. A HUMAN CHORIOCARCINOMA XENOGRAFT IN NUDE MICE; A MODEL FOR THE STUDY OF ANTIBODY LOCALIZATION.

Searle F, Boden J, Lewis JC, Bagshawe KD
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Br J Cancer; 44(2):137-144 1981

The successful development of the concept of linking cell-killing agents to tumor-specific antibodies will be largely determined by the extent to which the antibodies are preferentially localized in the malignant tissue. A xenograft of human choriocarcinoma (CC3) has been established in nude mice, and the relative distribution of affinity-purified specific antibodies to human chorionic gonadotrophin has been compared with that of nonspecific antibodies from the same species. Treatment of the nonspecific antibodies with ammonium thiocyanate appeared to be important to ensure that the distributions in normal nude mice were equivalent. Specificity indices, derived from the comparative distributions of isotope activity in the tumor and lung of labeled specific and nonspecific antibodies, ranged between 1.3 and 2.0. (Author abstract) (18 Refs)

30. IMMUNOHISTOLOGICAL ANALYSIS OF HODGKIN'S AND STERNBERG-REED CELLS: DETECTION OF A NEW ANTIGEN AND EVIDENCE OF SELECTIVE IGG UPTAKE IN THE ABSENCE OF B CELL, T CELL AND HISTIOCYTIC MARKERS.

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J Cancer Res Clin Oncol; 101(1):125-134 1981

The results of studies to clarify the origin and nature of Hodgkin's (H) and Sternberg-Reed (SR) cells are presented. Cytoplasmic IgG (CIgG) was demonstrated by immunostaining in polymorphic astrocytomas, liver cell carcinomas, and other polymorphic neoplasms as well as in H and SR cells. In addition, human IgG was taken up by rat liver cells, but alpha1 antitrypsin was not. These results showed that CIgG cannot be used as a marker for histiocytes. Staining of frozen sections revealed that H and SR cells lacked surface Igs and peripheral T-cell antigen. An antiserum raised against Hodgkin's disease (HD) L 428 cells and absorbed with normal human cells reacted strongly with H and SR cells in frozen sections of HD-affected lymph nodes. In 10 cases, the antiserum stained the surface of the H and SR cells; in 2 cases, it also stained the nucleoli and some chromatin spots. The antiserum did not react with tonsil tissue cells (lymphoid cells, histiocytes, interdigating reticulum cells). It was concluded that the nature of the H and SR cells is still open and that these cells might express antigens that have not yet been detected on normal cells. (29 Refs)

31. DIAGNOSIS OF BREAST CARCINOMA WITH THOMSEN-FRIEDENREICH (T) ANTIGEN AND HUMAN ANTI-T ANTIBODY.

Springer GF, Murthy SM, Desai PR, Wurtz K, Black S, Scanlon EF
Dept. Surgery, Northwestern Univ., Evanston, IL
Breast; 7(3):24-30 1981

Delayed-type skin hypersensitivity (DTH) to T antigen was measures in 102 patients with ductal breast carcinoma, 24 patients with lobular and two patients with tubular breast carcinoma, and 148 patients with benign breast diseases. Cell-mediated T antigen immunity was measured in vitro by leukocyte migration inhibition. T-specific immunoreactive structures were found on 93% of breast carcinoma tissues, all distant metastasis tissues, all cultured breast carcinoma-derived cell lines, on adenocarcinoma tissues from other sites, and on four out of six melanomas. T-specific structures were not detected in 29 of 31 benign breast lesions or any of four mammoplasty tissues. Patients showing apparent false positives had hyperplastic conditions, which were later rediagnosed as carcinomas. Data from patients after surgery suggest that T-specific DTH may be useful in monitoring treatment of breast cancer treatment, since DTH disappears in patients not showing recurrence of tumors. Apparently T-specific structures occur in normal tissues in a covered form. In adenocarcinoma tissues these structures are in an exposed, reactive form, which may serve diagnostic purposes. The T antigen may be useful in adjuvant therapy. (31 Refs)

32. EX VIVO PERFUSION OF A TUMOR-CONTAINING COLON WITH MONOCLONAL ANTIBODY.

Sears HF, Herlyn D, Herlyn M, Grotzinger PJ, Steplewski Z, Gerhard W, Koprowski H
Fox Chase Cancer Center, Central and Shelmire Ave., Philadelphia, PA, 19111
J Surg Res; 31(2):145-150 1981

We describe a model for the evaluation of antitumor antibody specificity using a colonic adenocarcinoma-containing specimen, freshly resected from a patient. The colonic segment was perfused for 1 hr through the mesenteric vessels with a perfusate soln containing an ACRC antibody known to bind specifically to cells of human colorectal carcinoma. Differential binding of a monoclonal ACRC antibody to cells of the adenocarcinoma and not to those of normal colonic mucosa was observed in three patients, whereas in two patients such differences in preferential binding were not observed. No antibody binding to any tissues was observed in the sixth patient. These results warrant further trial of in vivo evaluation of the specificity of ACRC antibody for diagnosis and therapy of human malignancy. (Author abstract) (7 Refs)

33. TUMOR-SPECIFIC ANTIBODIES IN SERA FROM PATIENTS WITH SQUAMOUS CELL CARCINOMA OF THE UTERINE CERVIX. DETECTION BY A MEMBRANE IMMUNOFLUORESCENCE ASSAY ON CULTURED CERVICAL CARCINOMA CELLS.

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Cancer Immunol Immunother; 11(3):201-206 1981

The possibility that circulating tumor-specific antibodies represent a diagnostic marker for the development of invasive cervical carcinoma (ICC) was studied. Sera were obtained from 74 patients with ICC, from 49 patients with early and preneoplastic stages (microinvasive carcinoma, carcinoma-in-situ, and dysplasia), from 65 controls without malignancy, and from 5 patients with non-ICC malignancies. Cervical cell carcinoma ME-180 cells were used as target cells. Sera were tested with an indirect immunofluorescence assay, by incubation with 0.1 mg/ml fluorescein-isothiocyanate (FITC)-labeled protein A which reacts with IgG or with FITC-labeled rabbit antihuman immunoglobulin antiserum diluted 1:30. Positive results were obtained from 63 (85%) of the ICC patients and 37 (57%) of controls. After absorption by tonsillar cells to remove non-specific antibodies, 61 (82%) of the ICC patients and 5 (8%) of the controls gave positive results. Patients with early and preneoplastic stages of cervical carcinoma did not differ significantly from controls. Evidently the antibody tested is specific for cervical carcinoma, but cannot be used as a diagnostic marker for early stages of the disease. Significance of the antibody in vivo is not known. (31 Refs)

IMMUNOGLOBULIN STRUCTURE AND SYNTHESIS

34. IN VITRO REGULATION OF IMMUNOGLOBULIN SYNTHESIS AFTER MARROW TRANSPLANTATION. I. T-CELL AND B-CELL DEFICIENCIES IN PATIENTS WITH AND WITHOUT CHRONIC GRAFT-VERSUS-HOST DISEASE.

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Blood; 58(3):431-439 1981

Twenty-four patients with aplastic anemia or acute leukemia were treated by marrow grafts from HLA-identical donors after conditioning with high doses of cyclophosphamide and/or total body irradiation. They were studied between 4 and 63 mo (median 14.2) after transplantation. Seventeen patients had chronic graft-versus-host disease (C-GVHD) and 7 were healthy. They were studied for defects in their T- and B-cell function using an indirect hemolytic plaque assay for Ig production after 6 days of culture in the presence of pokeweed mitogen. T or B cells from the patients with or without C-GVHD were cocultured with T or B cells from their HLA-identical marrow donors or unrelated normal controls. Intrinsic B-cell defects, lack of helper T-cell activity, and suppressor T-cell activity were more frequently found in patients with C-GVHD than in healthy patients. Fifteen of the 17 patients with C-GVHD showed one or more defects in their T- and B-cell function compared to only 3 of the 7 patients without C-GVHD. None of the healthy controls, including the marrow donors, showed defects in their T- and B-cell functions. These in vitro findings may be helpful in assessing the process of immune reconstitution and the immunologic aberrations found after human marrow transplantation. (Author abstract) (29 Refs)

35. IMMUNOGLOBULINIC FRAGMENTS OF URINARY PROTEINS IN PATIENTS AFFECTED BY ACUTE PNEUMOPATHIES, LUNG CANCER, AND TUBERCULOSIS.

Scrobogna S, Vriz G, Torre R, Trani S, Novello E, Panfili E
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Quad Sclavo Diagn; 17(1):31-39 1981

Electrophoretic and immunoelectrophoretic tests were performed on 95 urine samples of patients with lung cancer (15), bronchopneumonia (15), active tuberculosis (10), decompensated cardiopathy (10), chronic nephropathy (5), and chronic bronchitis (40). Of the 15 lung cancer patients 11 had the highest gamma globulin concentrations. Gamma fraction represents 20-40% of total proteins. Immunoelectrophoresis revealed a pattern: absence or only traces of alpha and mu anti-gamma, but marked increase in anti-lambda and kappa precipitation [F(ab) and Fc]. Proteins migrating in the gamma position are mostly fragments with mol wt below albumins. An increase in immunoglobulin synthesis and catabolism is apparent. End to inflammatory processes was preceded by disappearance of abnormal proteins; reduction in urinary immunoglobulinic fragments occurred after surgical removal of neoplasia and after immunosuppressive therapy. (21 Refs) (In ITA)

36. SECRETORY-COMPONENT-PRODUCING LUNG CANCER WITH HYPERGAMMAGLOBULINEMIA OF SECRETORY IGA.

Gotoh T, Takishita Y, Doi H, Tsubura E
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Cancer; 48(8):1776-1782 1981

Studies were made on a case of well-differentiated adenocarcinoma of the lung in which the serum levels of secretory IgA (sIgA) were very high. Immunofluorescent studies showed that secretory component (SC) was found to be diffusely distributed in cancer cells. The SC was detected in the supernatant of homogenates of cancer tissues from the primary site and lymph node with metastases. The SC extracted from cancer tissue and purified colostral SC were antigenically identical. The authors conclude that the adenocarcinoma cells produced SC and secreted it into the bloodstream and that the binding of SC with polymeric IgA resulted in the hypergammaglobulinemia of sIgA. This appears to be the first reported case of SC-producing lung cancer. The authors' findings suggest that the high serum levels of sIgA in cancer patients may be due to the production and secretion of SC by tumor cells themselves rather than the reabsorption of intraluminal sIgA into the circulation through a damaged epithelium. (Author abstract) (28 Refs)

37. A HUMAN B-CELL LYMPHOMA SYNTHESIZING AND EXPRESSING SURFACE MU-CHAIN IN THE ABSENCE OF DETECTABLE LIGHT CHAIN.

Gordon J, Hamblin TJ, Smith JL, Stevenson FK, Stevenson GT
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Blood; 58(3):552-556 1981

Lymph node cells obtained from a case of non-Hodgkin's lymphoma, of follicular center cell histology, were seen by immunofluorescence to express Ig mu heavy chains but no detectable light chain on their surfaces. Antibody specific for determinants expressed only on uncombined mu-chain reacted with these cell surfaces, but not with normal or neoplastic cells expressing surface IgM. Analysis of radioiodinated surface material revealed mu-chains which, without reduction, migrated on SDS-gel electrophoresis as normal mu-chain monomers, and again failed to detect light chains. Lysates of cells incubated with 3H-leucine revealed the synthesis of mu-chains but not of light chains. The labeled mu-chains were not secreted into the culture supernatant, a finding confirmed in parallel cultures by radioimmunoassay. The findings are discussed with particular reference to current concepts of the 'mu-chain only' phenotype. (Author abstract) (35 Refs)

38. THREE MONOCLONAL IMMUNOGLOBULINS, AN IGG2(KAPPA), AN IGM(KAPPA) AND AN IGM/A HYBRID, IN ONE PATIENT. I. ISOLATION AND CHARACTERIZATION.

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Immunology; 44(2):257-263 1981

Three monoclonal Ig components were identified in the plasma of a patient exhibiting a multiple gammopathy. These were an IgG2(kappa) and IgM(kappa) and an IgM/A hybrid molecule containing mu, alpha, and kappa antigenic determinants. This is the first report of an Ig hybrid which consists of portions of two different heavy-chain classes, and the significance of this observation in terms of our present concept of Ig gene arrangement is discussed. (Author abstract) (25 Refs)

39. IMMUNOHISTOLOGICAL ANALYSIS OF HUMAN LYMPHOID TISSUE BY DOUBLE IMMUNOENZYMATIC LABELLING.

Mason DY, Stein H, Naiem M, Abdulaziz Z
Haematology Dept., Level 4, John Radcliffe Hosp., Oxford OX3 9DU, England
J Cancer Res Clin Oncol; 101(1):13-22 1981

A double immunoenzymatic labeling technique for the visualization of pairs of antigens on human lymphoid tissue is described along with its application to paraffin-embedded and cryostat sections of normal or neoplastic tissues. The technique is based on the reaction of rabbit anti-alkaline phosphatase (AP) with an AP substrate and the reaction of goat, sheep, or, preferably, rabbit and mouse monoclonal antibodies with a peroxidase substrate. Cells containing both immunoglobulin (Ig) kappa and lambda chains, cells containing Ig and albumin, and cells containing IgM and IgG were detected in double-labeled paraffin sections. The cells that stained for both Ig light chain classes included Reed-Sternberg and Hodgkin's cells and the giant cells in non-Hodgkin's lymphomas. The double IgM/IgG cells were rare in nonneoplastic tissue and were not found in any of the greater than 100 non-Hodgkin's lymphomas studied. The double staining of cryostat sections with monoclonal antibodies enabled the simultaneous visualization of a variety of antigen pairs (eg, T-cell antigens and IgD). The greater preservation of antigenic reaction in the cryostat sections (compared with the paraffin sections) coupled with the wide range of antigens potentially detectable with monoclonal antibodies suggested that future studies in this area will add greatly to the knowledge of the human lymphoid system. (19 Refs)

40. EXPRESSION OF 2 IMMUNOGLOBULIN ISOTYPES, IGM AND IGA, WITH IDENTICAL IDIOTYPE IN THE B CELL LYMPHOMA I.29.

Sitia R, Rubartelli A, Hammerling U
Dept. Immunology, Univ. Genoa, Viale Benedetto XV, 10, 16132 Genoa, Italy
J Immunol; 127(4):1388-1394 1981

The I.29 tumor originated in I strain mice as a B cell lymphoma. In its ascitic form, the cells express Ia and Lyb antigens and carry the Fc receptor. The tumor cells synthesize two Ig, IgM and IgA, which have lambda-chains and heavy chain idiotypic determinants in common. Double labeling of viable cells in immunofluorescence demonstrates that a majority of cells have only IgM (mu+), a proportion has only IgA (alpha+), and a small population (usually less than 5%) expressed both Ig isotypes (mu+ alpha+). Although the relative proportions of mu+, alpha+, and mu+ alpha+ cells fluctuate quite markedly in the serial passages of the tumor, the three different subpopulations are consistently observed. The proportion of cells binding fluorescein-labeled anti-mu and rhodamine-labeled anti-alpha simultaneously in the cytoplasm is slightly higher (less than 10%). The appearance of cytoplasmic staining as brightly fluoresceinating granules suggests sequestration of Ig, possibly into vesicles. In vitro culture of I.29 cells rapidly leads to preferential expression of IgA only. This conversion from IgM- to IgA-producing cells was also observed when cultures were initiated with highly purified IgM+IgA- I.29 cells, suggesting differentiation rather than selective growth as the cause of the change. Cloning of I.29 cells by the limiting dilution technique yielded only cell lines of IgM-IgA+ phenotype. Implantation of one such cell line in nude mice produced a tumor that retained this phenotype in successive passages. (Author abstract) (57 Refs)

41. CELL-SPECIFIC CYTOTOXICITY EXPRESSED BY A CONJUGATE OF RICIN AND MURINE MONOCLONAL ANTIBODY DIRECTED AGAINST THY 1.1 ANTIGEN.

Houston LL, Nowinski RC
Dept. Biochemistry, Univ. Kansas, Lawrence, KS, 66045
Cancer Res; 41(10):3913-3917 1981

The isolation and characterization are described of a conjugate between ricin and a Thy 1.1-specific monoclonal IgG2a murine antibody synthesized using N-succinimidyl-3-(2-pyridyldithio)propionate. The conjugate selectively inhibited protein synthesis in Thy 1.1-positive (AKR SL3) mouse leukemia cells compared to Thy 1.2-positive (AKR/Cu SL1) cells. (Author abstract) (17 Refs)

42. T CELLS WITH FC RECEPTORS FOR IGA: INDUCTION OF TALPHA CELLS IN VIVO AND IN VITRO BY PURIFIED IGA.

Hoover RG, Dieckgraefe BK, Lynch RG
(c/o Lynch) Dept. Pathology (ML-144), Univ. Iowa Hosp., Iowa City, IA, 52242
J Immunol; 127(4):1560-1563 1981

Previous studies demonstrated that BALB/c mice with the IgA-secreting plasmacytomas MOPC-315 (alphalambda2), MOPC-167 (alphakappa), McPC-603 (alphakappa) and TEPC-15 (alphakappa) developed large numbers of T cells with surface membrane receptors for IgA (Talpha cells). The lack of Talpha cell expansion in mice with variant plasmacytomas that were nonsecretors or low secretors of IgA implied that elevated serum IgA contributed to the increase in Talpha cells. The present studies showed that normal BALB/c mice that were given daily injections of 30 mg of IgA (M315 protein) develop a marked increase in the number of Talpha cells. These studies also show that the Talpha cells induced by injection of IgA are Lyt1-2+ T cells. In addition, the data presented demonstrate that nylon wool nonadherent T cells, treated with purified polymeric IgA (M315 protein) in vitro, develop a marked increase in the number of Talpha cells. The in vitro induction of Talpha cells by IgA requires DNA and protein synthesis. These findings indicate that Talpha cell expansion observed in mice with IgA myeloma is related to the high serum level of IgA and not to the myeloma tumor per se. In addition, these observations have a more general relevance to the issue of B cell regulation because they demonstrate that secreted Ig can directly induce expansion of immunoregulatory T cells. (Author abstract) (17 Refs)

43. A VARIANT OF THE DEXTRAN-BINDING MOUSE PLASMACYTOMA J558 WITH ALTERED GLYCOSYLATION OF ITS HEAVY CHAIN AND DECREASED REACTIVITY WITH POLYMERIC DEXTRAN.

Matsuuchi L, Wims LA, Morrison SL
Dept. Microbiology, Columbia Univ., Coll. Physicians and Surgeons, New York, NY, 10032
Biochemistry; 20(17):4827-4835 1981

Variants have been isolated from the J558 BALB/c mouse myeloma (IgA, lambda; anti-alpha1 3dextran) that are producing immunoglobulin Ig altered in reactivity with polymeric dextran. In this report, one spontaneously raising mutant, L187, is characterized in detail. The Ig produced by L187 was indistinguishable in mol wt from that of J558; however, a difference in charge between the two proteins was observed and could be localized to the Fab portion of the molecule. Peptide map analysis failed to shown any differences between the amino acid content of the proteins; instead, the carbohydrate content of the chains differs. Examination of the glycopeptides derived from J558 and L187 Igs showed that L187 glycopeptides contain more sialic acid. Altered glycosylation apparently was the consequence of altered glycosyl-transferases within the two cell lines. Comparison of the glycopeptides from the glycoprotein G of vesicular stomatitis virus (VSV) grown in mutant and wild-type cells shows that the mutant and wild-type cells differ in their cellular glycosyltransferases. Somatic cell hybrids between either L187 or J558 and MPC-1 1 (4T001) also demonstrate that in the proper cellular environment the J558 protein could contain large amounts of sialic acid. J558 protein, synthesized in the hybrids and containing sialic acid, bound antigen less well than did wild-type J558 protein and identically with L87 protein synthesized in the somatic hybrids. L187 Ig does not react with polymeric dextran as well as does J558 Ig. However, the mutant Ig appears to have the same reactivity pattern with oligosaccharides as does J558, and thus the size of its antibody combining site does not appear to differ from that of J558. L187 shows that different myeloma cell lines and mutants may have different glycosyltransferases available and provides the first demonstration that the carbohydrate content of an Ig molecule can influence its reactivity with antigen. (Author abstract) (52 Refs)

44. RECOGNITION OF MOPC-460 VARIABLE REGION DETERMINANTS BY POLYCLONALLY DISTRIBUTED TRIGGERING RECEPTORS ON B LYMPHOCYTES.

Primi D, Juy D, Le Guern C, Sanchez P, Cazenave PA
Unite d'Immunochimie Analytique, Institut Pasteur, 28 rue du Dr. Roux, 75724 Paris Cedex 15, France
J Immunol; 127(4):1714-1718 1981

Purified M460 protein-induced untreated and anti-Thy 1.2 and complement-treated murine spleen cells to proliferate and differentiate in vitro. Fc receptor complexing was not responsible for the phenomenon, since M460 Fab fragments retained the B cell triggering activity. Activation was inhibitable by the addition of DNP-glycine to cultures and could also be detected by using spleen cells from various strains of mice, including the C3H/HeJ, which is genetically nonresponding to LPS. Hybrid molecules were constructed between the M460 proteins and the products of two myelomas that do not activate B cells, namely, X25 and X24. The only hybrid molecules that retained triggering activity were (L460-HX25)2. Interestingly, the same molecule was also the only one recognized by an anti-M460 monoclonal antibody (F6(51)) that has been previously shown to induce B cells to proliferate and differentiate. The data suggest the existence on B lymphocytes of a network of polyclonally distributed mitogen receptors that share determinants cross-reacting with Ig idiotypes. (Author abstract) (21 Refs)

45. RAT IGD MYELOMA PROTEIN: CELL-FREE TRANSLATION OF THE DELTA MRNA AND BIOCHEMICAL ANALYSIS OF INTRACELLULAR AND MEMBRANE DELTA CHAIN.

Sire J, Alcaraz G, Bourgois A, Jordan B
Centre d'Immunologie INSERM-CNRS de Marseille-Luminy, Case 906, F-13288 Marseille Cedex 9, France
Eur J Immunol; 11(8):632-636 1981

The analysis of IgD molecules produced by the tumor-derived IR 731 cell line showed that these molecules are not secreted and are only present at the cell surface as covalent dimers of 48,000 dalton delta chains. The original IR 731 tumor secreted complete IgD; thus, the disappearance of secretion in the cell line was correlated with the absence of light chain synthesis. The mRNA coding for the cell line delta chain was isolated and translated. The analysis of the translated delta chain (mol wt: 40,000) confirmed the absence of a region having the size of a domain as previously shown by partial amino acid sequence. The observation that the absence in delta chain of this region, which comprises most of the CH2 domain, could be a general feature of murine species is discussed. (Author abstract) (48 Refs)

HUMORAL IMMUNE BLOCKING FACTORS AND ANTIGEN-ANTIBODY COMPLEXES

46. INFLUENCE OF IGG AND IGM RECEPTOR TRIGGERING ON HUMAN NATURAL KILLER CELL CYTOTOXICITY MEASURED ON THE LEVEL OF THE SINGLE EFFECTOR CELL.

Merrill JE, Ullberg M, Jondal M
Dept. Tumor Biology, Karolinska Institutet, S-104 01 Stockholm, Sweden
Eur J Immunol; 11(7):536-541 1981

By using an agarose single cell cytotoxicity assay, in combination with rosetting with IgG- or IgM-coated ox RBC for detection of Fc receptors for IgG (FcgammaR) or IgM (FcmuR), it was found that 60% of natural killer (NK) cells are FcgammaR+ and 17% FcmuR+. This system was further used to investigate the consequence of FcuR and FcgammaR triggering on NK killing as measured on the single effector cell level. It was found that stimulation of the FcgammaR, but not the FcmuR, resulted in substantial NK inhibition. In order for NK cells to be inhibited by IgG-coated ox RBC, they must first be exposed to the IgG-containing complex prior to conjugation with the target. While exposure of the FcgammaR to immune complexes can block up to 57% of NK activity, the particulate immune complexes do not interfere with binding of effector cells to targets. Modulation of FcgammaR by capping at 37 C does not interfere with the NK inhibition for up to 3 hr, though after 20 hr, when FcgammaR+ cells are almost completely modulated, NK activity has fully returned. Although to a lesser extent, the soluble immune complex human transferrin-anti-transferrin also reduces NK cell activity when activating effector cell FcgammaR prior to target cell binding. Also, pretreatment of target cells with high concentrations of specific antibody toward membrane antigens can block NK activity while not inhibiting target cell binding as evidenced by anti-IgM IgG binding to Daudi cells. The regulatory influence of the FcgammaR on the NK system is discussed in terms of other functions associated with this receptor and in terms of its possible biological significance. (Author abstract) (25 Refs)

47. EVOLUTION AND CHARACTERIZATION OF RENAL IMMUNE COMPLEXES DEPOSITION IN MICE BEARING A SYNGENEIC TUMOR.

Leyva-Cobian F, Lamoureux G, Rojo-Ortega JM
Dept. Immunology, Centro Ramon y Cajal, Madrid-34, Spain
Renal Physiol; 4(2/3):79-84 1981

Experiments were undertaken to determine(1) the chronology of the appearance of immune complexes (IC) in the mesangium and along the glomerular basement membrane (GBM) in mice bearing B16 melanoma, (2) the electron microscopic characterization of these deposits, and (3) if surgical excision of the tumor would be followed by disappearance of the IC. Male C57BL/6 mice were divided into three groups. In group I, 10 animals were unilaterally nephrectomized (right kidney) at 7, 14, or 21 days after tumor inoculation and the tumor was simultaneously removed. Group II was treated as group I, except that they were never inoculated. Group III was treated as group I, except that the tumors were not removed. B16 melanoma grew in 100% of the inoculated mice. Renal glomeruli of the inoculated mice showed mild proliferative glomerulonephritis. IgA deposits did not give a consistent pattern. IgG, IgM, and complement component C3 were found by their immunofluorescence (IF) on the mesangium and GBM of 100% of the affected mice. with IgG being the most prominent. When the left kidneys were examined at autopsy, the IC deposits in mice of group I decreased after tumor removal: after tumor removal in 14-day-old tumor-bearing mice, the IF for IgG became negative in 80% and the IF for IgM became negative in 60% of the mice. These changes did not occur in mice of group III. (21 Refs)

HUMORAL IMMUNOSUPPRESSIVE AGENTS

48. IMMUNOSUPPRESSIVE EFFECT OF CYCLOPHOSPHAMIDE ACTIVATED IN VITRO BY LIVER MICROSOMES FROM MICE OF DIFFERENT STRAINS.

Telegin LIu, Zhirnov GF, Mazurov AV, Pnevnitskii LA
Lab. Immunogenetics, Inst. Medical Genetics, Moscow, USSR
Biull Eksp Biol Med; 91(7):57-60 1981

To test the hypothesis that the differences in the immunosuppressive activity of cyclophosphamide (CP) are due to the interstrain differences in the sensitivity, CP was incubated with liver microsomes from CBA, BALB/c, and DBA/2 mice. The max rate of CP hydroxylation during incubation of liver microsomes from BALB/c mice was correlated with the highest content of cytochrome P 450. (18 Refs) (In RUS)

OTHER RELATED STUDIES

49. IMMUNOLOGIC REACTION TO ORAL CANCER.

Toto PD, Bromberg MJ, Toto M
Dept. Oral Pathology, Loyola Univ. Sch. Dentistry, 2160 South First Ave., Maywood, IL, 60153
Oral Surg; 52(3):327-332 1981

Oral squamous cell carcinoma in human beings and that induced in the hamster pouch with DMBA both show a lymphocytic reaction in the lamina propria. Serum from the hamsters reacts with the epithelium in the cancer but not in the normal mucosa, suggesting a humoral response in DMBA-induced cancer cell transformation. (Author abstract) (13 Refs)

50. THE EFFECT OF BESTATIN ON THE LYMPHOCYTE FUNCTIONS OF CANCER PATIENTS.

Noma T, Yata J, Hoshi K, Ishii T
Dept. Pediatrics, Tokyo Medical and Dental Univ., Tokyo, Japan
Nippon Gan Chiryo Gakkai Shi; 16(3):453-459 1981

Bestatin was administered to 31 patients with digestive tract cancer before any other therapeutic treatment. The drug enhanced the helper function of T cells in immunoglobulin (Ig) production in approx one-half of the patients, and it activated mitomycin C-sensitive T cells that suppressed Ig production in most patients. In approx one-third of the patients, bestatin also augmented the natural killer and cytotoxicity activity of T cells against allogeneic target cells. (23 Refs) (In JPN)

51. IMBALANCE OF T-CELL SUBPOPULATIONS DOES NOT RESULT IN DEFECTIVE HELPER FUNCTION IN CHRONIC LYMPHOCYTIC LEUKEMIA.

Inoshita T, Whiteside TL
(c/o Whiteside) Dept. Pathology, Univ. Pittsburgh, Sch. Medicine, 406 Scaife Hall, Pittsburgh, PA, 15261
Cancer; 48(8):1754-1760 1981

The T-lymphocyte subpopulations identified by the Fc receptors for IgG (TG cells) and IgM (TM cells) in 12 patients with B-cell chronic lymphocytic leukemia (CLL) were quantitated and studied for functional capabilities in an in vitro assay. The TG cells in patients were elevated in relation to age- and sex-matched normal controls (p less than 0.05) resulting in an altered TM/TG ratio of 1.8 +-0.76 in CLL versus 5.9 +-3.7 in controls (mean +- SD, p less than 0.001). Despite this altered TM/TG ratio, the functional capability of the CLL T cells to regulate the terminal differentiation of B cells was found to be normal as reflected by the mean helper-suppressor score of 0.77 +-0.13 (+- SEM) obtained for both patients and controls. This unimpaired capacity of the T cells from CLL patients to help normal B cells mature into Ig-secreting cells indicated that hypogammaglobulinemia and monoclonal serum Ig in these patients may be a result of either an intrinsic defect in the B lymphocytes or their replacement by a neoplastic clone rather than a defect in the immunoregulatory T cells. (Author abstract) (39 Refs)

52. PATTERNS OF ANTIBODY REACTIVITY AGAINST SELECTED HUMAN LEUKEMIA CELL LINES.

Anderson MJ, Oeljeschlager H, Muller-Hermelink HK, Muller-Ruchholtz W
(c/o Muller-Ruchholtz) Dept. Immunology, Univ. Kiel, Brunswiker Strasse 2-6, D-2300 Kiel, W. Germany
J Cancer Res Clin Oncol; 101(1):101-107 1981

The cross reactivity of rabbit antilymphocyte serum (ALS) with human bone marrow (BM) cells and with a panel of human leukemia cell lines was analyzed following various absorption procedures. Initially, the BM cells were labeled with immunoperoxidase after incubation with unabsorbed ALS or ALS sequentially absorbed with fresh human RBC, chronic myelogenous leukemia cells, and fetal liver cells. Antibodies reacting with all BM cell populations were present in the unabsorbed ALS, but those reacting with nonlymphoid cells were progressively eliminated by the absorption procedure. The labeling pattern of cells incubated in ALS absorbed with the individual leukemia cell lines showed that antibodies reacting with early erythropoietic cells, late myelopoietic cells, and granulocytes were eliminated by absorption with most of the cell lines. Triple combination absorptions with specific cell lines produced an ALS that was specific for pre-T and mature T cells. These results confirmed the feasibility of preparing an an ALS with the requisite sensitivity for application in BM transplantation. (6 Refs)

53. STIMULATORY EFFECTS ON VARIOUS IMMUNOLOGIC RESPONSES BY ASCITES FLUIDS FROM PATIENTS WITH METASTATIC MALIGNANCY.

Wang BS, Heacock EH, Collins KH, Saporoschetz I, Steele G, Mannick JA
Dept. Surgery, Brigham and Women's Hosp., Harvard Medical Sch., Boston, MA, 02115
Clin Immunol Immunopathol; 21(1):83-93 1981

Cancer ascites has been repeatedly shown to suppress a number of immune responses. In this report, we examined a total of 28 unfractionated ascitic fluid samples from patients with various metastatic malignancies and rather unexpectedly found that the majority of these samples were capable of enhancing various immune reactivities. Twelve of 17 samples were shown to increase significantly humoral antibody production in mice when injected 1 day before sheep RBC. Ten of 13 samples significantly enhanced the proliferative response of human peripheral blood mononuclear WBC to the T-lymphocyte mitogen, phytohemagglutinin. Twelve ascitic samples were added to mouse mixed lymphocyte cultures and 9 were found to augment significantly the generation of alloreactive cytolytic lymphocytes. Pooled normal human serum was similarly tested as a control and found to have no effect in these systems. Furthermore, we have isolated three active fractions from these cancer ascites fluids by Sephadex G-75 gel filtration. However, each fraction was predominantly responsible for enhancing only one of the three immune responses tested. (Author abstract) (16 Refs)

54. ERADICATION OF DISSEMINATED MURINE LEUKEMIA BY CHEMOIMMUNOTHERAPY WITH CYCLOPHOSPHAMIDE AND ADOPTIVELY TRANSFERRED IMMUNE SYNGENEIC LYT-1+2-LYMPHOCYTES.

Greenberg PD, Cheever MA, Fefcr A
Div. Oncology, Dept. Medicine, Univ. Washington Sch. Medicine, Seattle, WA, 98195
J Exp Med; 154(3):952-963 1981

The efficacy of T cell subpopulations, as distinguished by expression of Lyt antigens, was analyzed in adoptive chemoimmunotherapy (ACIT) of established murine leukemia and in in vitro assays for the generation and expression of cytotoxicity. The results demonstrated that the predominant donor effector cell required for eradication of advanced disseminated leukemia by ACIT is an immune Lyt-1+2-T cell that is not cytolytic in vitro. Immune cells depleted of Lyt-2+ cells, such that the only donor T cells remaining were of the Lyt-1+2-phenotype, were nearly as effective in ACIT as unselected cells suggesting that other donor T cell subsets do not provide an essential contribution. The potential therapeutic efficacy of immune cells was ablated nearly as completely by depletion of Lyt-1+ cells as by depletion of all T cells. The small residual anti-tumor effect still evident after treatment of immune cells with alpha-Thy-1.2 and complement probably reflected incomplete T cell removal. The T cell subset analyzed in ACIT were defined operationally by susceptibility to lysis by monoclonal antibody to Lyt antigens and complement. The results demonstrated that the phenotype of the predominant T cell subset required for efficacy in ACIT is Lyt-1+2-, which is distinct from the T cell phenotypes mediating in vitro tumor lysis. The mechanisms by which Lyt-1+2-cells can promote tumor rejection are discussed. (31 Refs)

55. POLYVALENT PNEUMOCOCCAL IMMUNIZATION OF PATIENTS WITH PLASMA CELL DYSCRASIAS.

Shildt RA, Rubin RR, Schiffman G, Giolma P
Oncology Service, Brooke Army Medical Center, Box 517, Beach Pavilion, Fort Sam Houston, TX, 78234
Cancer; 48(6):1377-1380 1981

Thirteen patients with plasma cell dyscrasias and 27 healthy adults were immunized with polyvalent pneumococcal vaccine. Antibody responses were determined by radioimmunoassay. Patients with plasma cell disorders had significantly lower preimmunization and postimmunization antibody titers compared with those of the controls (p-0.01 and 0.008, respectively). Even though the overall response in myeloma patients was poor, occasional rises in antibody titers occurred. Immunizing myeloma patients with the pneumococcal vaccine is recommended. (Author abstract) (16 Refs)

56. HODGKIN'S DISEASE: ESTABLISHMENT AND CHARACTERIZATION OF FOUR IN VITRO CELL LINES.

Diehl V, Kirchner HH, Schandt M, Fonatsch C, Stein H, Gerdes J, Boie C
Dept. Hematology/Oncology, Inst. Genetics, Sch. Medicine, Karl-Wiechert-Allee 9, D-3000 Hannover, W. Germany
J Cancer Res Clin Oncol; 101(1):111-124 1981

Four in vitro cells established from the pleural effusions of two Hodgkin's disease (HD) patients and from the blood and bone marrow of a third were characterized morphologically, immunologically, and biochemically. The malignant nature of the cultured cells was confirmed by the presence of structural and numerical chromosome abnormalities, the monoclonality of marker chromosomes, and the lack of Epstein-Barr virus-specific antigens. The cells gave rise to tumors in nude mice following intracranial transplantation and induced sc tumors when embedded on plasma dots before transplantation. All four lines were positive for Ia-like antigens, T-cell receptors, acid phosphatase, and acid esterase; they were negative for lysozyme peroxidase, chloracetate esterase, surface Ig or cytoplasmic Ig (CIg), and recep tors for complement 3b, complement 3d, IgG-FC, and mouse or sheep RBC. Except for the lack of CIg in the in vitro cells, the marker pattern corresponded to that of Hodgkin's and Sternberg-Reed cells in biopsy material. The phenotype was not that of B cells, T cells, myeloid cells, monocytes, or macrophages. (26 Refs)

57. CANCER AND SUBVERSION OF HOST DEFENCES.

Nelson DS, Nelson M, Farram E, Inoue Y
Kolling Inst. Medical Res., Royal North Shore Hosp., St. Leonards, N.S.W. 2065, Australia
Aust J Exp Biol Med Sci; 59(part3):229-262 1981

The relationship between cancer and the immune system is reviewed. Effector cells, defects in cell-mediated and humoral immunity in cancer patients, immune defects in experimental animals, stimulation of macrophages and other cells, and the subversion of host defenses by viruses are discussed. Soluble products of tumor cells, which may act directly on the cell or mediators involved in inflammation or indirectly by way of the immune system, seem to be key factors in the subversion of host defenses. Tumors may also subvert host defenses by inducing suppressor cell production. The ability of a host to promote tumor growth, interactions between the clotting systems and cell-mediated immunity, and activated macrophages serving as antitumor effector cells are described. It was suggested that there is a great deal of evidence that tumors can depress or subvert various components of the host's immune system. (268 Refs)

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TUMOR ANTIBODY PRODUCTION/ CHARACTERIZATION/ DETECTION

1. A NEW MOUSE CELL-SURFACE ANTIGEN (LY-M20) CONTROLLED BY A GENE LINKED TO MLS LOCUS AND DEFINED BY MONOCLONAL ANTIBODIES.

Kimura S, Tada N, Nakayama E, Liu Y, Hammerling U
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021

Immunogenetics; 14(1/2):3-14 1981

Five monoclonal antibodies were established by the fusion of mouse myeloma cells (NS.1) with spleen cells from A and (A x

HE 20.3173/2:

C3H/An)F1 mice hyperimmunized with 70Z/3 tumor cells. These antibodies recognized a new antigenic specificity provisionally called Ly-m20.2. In direct cytotoxicity assays, 60% of cells in spleen, 40% in lymph node, 50% in bone marrow and less than 5% in thymus were found to react with three of the five antibodies, whereas the two others yielded somewhat lower cytotoxicity indices. The Ly-m20.2 antigen was also expressed on cells derived from liver and kidney but not on cells derived from brain. As judged from cytotoxicity assays with separated T and B cells, Ly-m20.2 antigen is carried preferentially on B lymphocytes. Direct plaque-forming cells were completely eliminated by Ly-m20.2-specific antibody and complement. Linkage tests by analysis in 20 (CBA/J x C3H/An) x C3H/An backcross mice and by segregation analysis of BXH and SWXL recombinant inbred strains indicate close association of the loci controlling ly-m20.2 and Mls antigens on chromosome 1. (Author abstract) (30 Refs)

2. NUCLEOLAR IMMUNOFLUORESCENCE IN BONE MARROW SPECIMENS OF HUMAN HEMATOLOGICAL MALIGNANCIES.

Smetana K, Busch RK, Hermansky F, Busch H
(c/o H. Busch) Dept. Pharmacology, Baylor Coll. Medicine, Houston, TX, 77030
Blut; 42(2):79-86 1981

Nucleolar immunofluorescence (NIF) produced with HeLa cell nucleoli antibodies was studied in three patients with acute myeloid leukemia (AML), four with chronic myeloid leukemia (CML), five with multiple myeloma (MM), and five with chronic lymphocytic leukemia (CLL: B-cell type). In CML, bright NIF was mainly observed in blastic cells. The percentage of such cells with NIF ranged from 10-80%. The appearance of such cells is described. Other stages of the granulocytic line in CML marrows, such as promyelocytes, myelocytes, and metamyelocytes usually did not contain NIF; in fluorescent cells, the NIF was less bright than in myeloblasts. Other CML bone marrow cells in the same specimens did not exhibit NIF including those identified as erythroblasts and megakaryocytes. In AML, bright NIF was also observed in a variable number of blastic cells whose fluorescent nucleoli resembled those of myeloblasts. The other bone marrow nucleated blood cells did not exhibit NIF. In MM, most cells that exhibited bright NIF were plasmacytes. The percentage of plasmacytes with NIF ranged from 3-82%. Large fluorescent nucleoli that were difficult to classify are described. All other cells in MM bone marrows did not exhibit bright NIF. Bright NIF was noted in groups of lymphocytes and solitary lymphocytes infiltrating CLL bone marrows. These cells usually contained one or two relative large fluorescent nucleoli; the number of nucleoli corresponded with that found after staining. The results indicated that NIF produced by incubation of bone marrow smears with HeLa cell nucleoli antibodies is limited to leukemic and myeloma cells. (15 Refs)

3. TUMOUR-ASSOCIATED ANTIGENS REACTING WITH CYTOTOXIC ANTIBODIES IN SERUM OF HEPATOMA-BEARING RATS.

Lando P, Berzins K, Gabriel J, Larsson P, Perlmann P
Dept. Immunology, Univ. Stockholm, S-10691 Stockholm, Sweden
Br J Cancer; 44(4):522-531 1981

The 3M-KC1 extracts of the hepatoma D23 contain antigens that inhibit the complement-dependent cytotoxicity for D23 hepatoma cells of serum from D23 tumor-bearing rats (D23 TBS). Inhibition was not due to a general anticomplementary activity of the extracts. Although a minor part (25%) of the protein of D23-KC1 extract was insoluble in PBS, this part contained most of the inhibitory activity. Fractionation of the PBS-soluble material of the extract on Concanavalin A-Sepharose showed that the inhibitory activity did not bind to the lectin. Analysis of D23-KC1 extracts on a Sepharose CL-4B column showed that the antigens involved in the cytotoxicity were heterogeneously distributed in the high-mol wt region (greater than 200,000). Precipitation with 10% trichloroacetic acid (TCA) of D23 KC1 extracts revealed that most of the antigenicity was insoluble in TCA. Heating of D23 KC1 extracts at 100 C did not affect the antigenicity. Enzyme treatment of D23 extra nuclear membranes (D23 ENP) revealed that the inhibitory activity was not sensitive to proteolytic digestion, while treatment with phospholipase A2, C or D abrogated partly the inhibitory activity. The lipid nature of the antigenicity was indicated by its solubility in organic solvents as chloroform or n-butanol. (Author abstract) (25 Refs)

4. SENSITIVITY IN DETECTION OF MONOCLONAL IMMUNOGLOBULINS BY THIN-LAYER ISOELECTRIC FOCUSING AND CERTAIN ELECTROPHORESES IN LABORATORY USE.

Kamiya-Harada Y, Sato Y, Otani H, Kawakami M
Molecular Biology Lab., Sch. Medicine, Kitasato Univ., Kitasato, Sagamihara, Kanagawa 228, Japan
Microbiol Immunol; 25(10):1067-1076 1981

The best hydrogen ion concentration range for detection of the band group specific for monoclonal immunoglobulin (MCIG) by thin-layer isoelectric focusing (IEF) was pH 5 to 8. Concentration of MCIG was estimated from the intensity of band staining. IEF was performed with patient sera containing myeloma proteins of various classes using pH gradient gels of different pH ranges. Lowest concentration of MCIG detected was approx 0.1 mg/ml, which was 8-32 times lower than the concentration detectable by cellulose acetate membrane electrophoresis (CAE) or immunoelectrophoresis (IE) in routine laboratory use. Intensities of the band stain in IEF showed a linear relationship with concentrations from 0.1-50.0 mg/ml. Blind tests on sera resulted in some disagreement between the concentration of MCIG from results with CAE and IE and those determined by IEF. Results suggested that IEF will be a useful method to detect early malignant monoclonal immunoglobulinemia after the technique and equipment are improved for laboratory tests. (17 Refs)

5. THE USE OF HEMOLYSIS-IN-GEL ASSAYS TO STUDY POLYCLONAL ANTIBODY SECRETION IN BON E MARROW TRANSPLANT RECIPIENTS.

Ringden O, Witherspoon RP, Storb R, Thomas ED
Div. Transplantation Surgery, Dept. Surgery, Huddinge Hosp., S-141 86 Huddinge, Sweden
Blut; 42(4):221-226 1981

B cell function was studied in 80 bone marrow transplant patients using direct and indirect assays of polyclonal antibody production. Patients included 24 with aplastic anemia and 56 with hematologic malignancies. Control included 48 marrow donors and 18 healthy, unrelated individuals. Direct assay (DA) measured plaque-forming cells (PFC) by hemolysis in gel with fluorescein isothiocyanate-coupled sheep RBC (FITC-SRBC) as targets. Indirect assay (IA) used protein A-coupled SRBC and antisera against human IgG, IgA, and IgM. Both assays indicated deficient B cell function in patients analyzed 3 mo after transplantation. IA of controls detected IgM-producing B cells 44 x as high as the level detected by DA. PFC for transplant patients after 1 yr differed from controls only in those cases with graft-versus-host disease (GVHD) having IgM deficiency. Staphylococcus aureus activation produced abnormally high PFC numbers in patients with GVHD. IgG and IgA after S aureus were higher after 3 mo in patients with infections than in patients without infection. IgG PFC in background cultures and after S aureus activation were higher in patients with HLA-nonidentical marrow donors than in those with HLA-identical donors. (9 Refs)

6. SURFACE ANTIGENS OF HUMAN MELANOMA CELLS DEFINED BY MONOCLONAL ANTIBODIES. I. BIOCHEMICAL CHARACTERIZATION OF TWO ANTIGENS FOUND ON CELL LINES AND FRESH TUMORS OF DIVERSE TISSUE ORIGIN.

Johnson JP, Demmer-Dieckmann M, Meo T, Hadam MR, Riethmuller G
Institut fur Immunologie, Schillerstr. 42, D-8000 Munchen 2, W. Germany
Eur J Immunol; 11(10):825-831 1981

Monoclonal antibodies were produced against melanoma cell lines derived from patients presently disease free. Based on tissue distribution of binding, the antibodies obtained could be used to classify melanoma surface antigens into groupings similar to those obtained from studies of autologous and xenogeneic antibodies. Three antibodies (21.43, 15.75 and 15.95) reacted with the immunizing tumor but not with peripheral blood lymphocytes or a lymphoblastoid cell line derived from the tumor donor. When tested on a broader cell panel, antibody 21.43 reacted only with melanoma lines, while antibodies 15.75 and 15.95 reacted with carcinoma cell lines as well as with the majority of melanoma cell lines. Antibody 15.95 precipitated a 49,000 dalton glycoprotein from both melanoma and carcinoma cells. Antibody 15.75 precipitated a 74,000 dalton glycoprotein from the surface of melanoma and carcinoma cell lines which is also found on freshly isolated tumor cells from melanoma and carcinoma metastases in vivo. (Author abstract) (30 Refs)

7. PHENOTYPIC HETEROGENEITY AND CELLULAR ORIGINS OF T CELL MALIGNANCIES.

Greaves MF, Rao J, Hariri G, Verbi W, Catovsky D, Kung P, Goldstein G
Membrane Immunology Lab., Imperial Cancer Res. Fund, Lincoln's Inn Fields, London WC2A 3PX, England
Leuk Res; 5(4/5):281-299 1981

The reactivity of the OKT series of monoclonal antibodies was compared with a panel of other monoclonal antibodies, sheep erythrocyte rosette formation, and expression of terminal deoxynucleotidyl transferase in untreated T cell malignancies. Also included in the series were OKT11 and OKT11A, two new monoclonal antibodies with pan-T activity. The composite phenotypes of cells from individual patients were classified according to a presumptive sequence of T lymphocyte differentiation. Six categories of T cell phenotypes were designated, four of thymic type and two of mature T cells. Cells from 82 untreated patients with T cell malignancy were tested with the OKT series of monoclonals and other markers. The OKT defined phenotype of 13 established T cell lines is presented. The most striking result from this analysis was the association between overall phenotype and diagnostic subgroup of T cell malignancy. The results indicated that T cell leukemias have exclusive, composite phenotypes which are in themselves remarkably heterogeneous. It was suggested that T-cell acute lymphoblastic leukemia and T-cell non-Hodgkin's lymphoma in young patients originate in a thymic stem cell with varying levels of maturation arrest, whereas those T malignancies in adults with a mature T cell phenotype arise from long-lived immunocompetent T cells. (79 Refs)

8. HUMAN MELANOMA-ASSOCIATED ANTIGENS; IMMUNOCHEMICAL AND MOLECULAR PROFILE.

Reisfeld RA, Galloway DR, Morgan AC, Walker LE, Bumol TF
Scripps Clinic and Res. Foundation, La Jolla, CA
Cancer Bull; 33(5):211-218 1981

Some of the immunochemical approaches taken in the authors' laboratory to isolate and characterize two human melanoma-associated antigens utilizing specific polyclonal and monoclonal antibodies are described. Analysis of cellular proteins released into the surrounding culture of several human melanoma cells lines indicated three major components detected by polyclonal antimelanoma xenoantisera with mol wt of 260K (260,000), 240K and 100K. The 240K component has been identified as fibronectin. The 100K component is found in spent media of both melanoma and carcinoma cell lines. The 100K and 260K dalton antigens which have affinity for specific lectins and metabolic radiolabeling with sugars strongly suggest they were glycoproteins. Other studies are reported on the use of monoclonal antibody for structural characterization, production of monoclonal antibody, subunit composition of 100K and 250K dalton melanoma antigens, and functional properties. It is apparent that the two melanoma-associated antigens of 100K and 250K dalton, defined immunochemically by monoclonal antibody, are likely to play a key role in the elicitation of host immune responses to malignant melanoma. Furthermore, it appears that changes in intracellular transport, glycosylation, and cell-surface expression of these two markers may be associated with neoplastic transformation. (12 Refs)

9. IMMUNOPEROXIDASE STUDIES ON A TUMOR-CELL-ASSOCIATED ANTIGEN(S) IN RAT RENAL NEOPLASMS INDUCED BY DIMETHYLNITROSAMINE.

Yantchev IK
Inst. General and Comparative Pathology, Bulgarian Acad. Sciences, Sofia-1113, Bulgaria
Neoplasma; 28(4):447-455 1981

Renal neoplasms were induced in rats of Wistar line by a single, ip injection of dimethylnitrosamine (60 mg/kg). The histological investigation indicated that these tumors were entirely mesenchymal in nature. In some of them (16.6%) small adenocarcinomas were seen. Immunological studies were carried out by light and electron microscope, using the immunoperoxidase 'bridge' technique. Tumor cell-associated antigen(s) was detected in 62% of the neoplasms examined. This antigen was individual as it did not react with sera from the other tumor bearing rats. It was established that this antigen was located mainly on the plasma membrane and also, even though in a lesser degree, on the endoplasmic reticulum and nuclear envelope of the tumor cells of mesenchymal and epithelial origin. Except the existence of tumor cell-associated antigen(s) in these neoplasms, the presence of antibodies produced against them in the sera of the diseased rats were also detected by these investigations. (Author abstract) (23 Refs)

10. PRODUCTION OF ANTIBODIES AGAINST ANTIGENS RELEASED FROM HUMAN PANCREATIC TUMOUR XENOGRAFTS.

Grant AG, Duke D
Dept. Surgery, St. George's Hosp. Medical Sch., London SW17 0RE, England
Br J Cancer; 44(3):388-395 1981

Antibodies directed against the antigens released from viable tumor cells during growth have been raised by cross-immunization of immunocompetent hairy litter-mates with serum from nude mice bearing pancreatic tumor xenografts. Antisera raised against the components released from a primary pancreatic tumor xenograft (WB) or from a tumor cell-line xenograft (GER) showed a titer greater than 1:625 against cultured pancreatic tumor cells by an I125-binding assay. Five out of 14 of the hairy litter-mates immunized with serum from the same tumor (GER) produced antisera that bound more strongly to pancreatic cancer cells than to 13 other non-pancreatic cell lines (binding ratio greater than 2). Absorption of the antisera with pure CEA reduced the level of binding by 11-25% without affecting the specificity for pancreatic tumor cells. The antibody response could be completely removed by absorption with pancreatic tumor cells, whereas 50% and 18% of the activity remained after absorption with normal pancreas homogenate and a mixed non-pancreatic tumor-cell pool, respectively. Immunofluorescent staining of pancreatic tumor sections indicated that the antibody was localized on the membrane of ductular epithelial cells. Challenge of immunocompetent mice using this procedure has produced a polyspecific antiserum with signs of selectivity for the circulating antigens released from pancreatic cancer cells, and may provide a route to the production of antibody against specific tumor components. (Author abstract) (31 Refs)

11. HUMORAL IMMUNE RESPONSE IN MELANOMA AND GLIOMA PATIENTS: A SOLUBILIZED MELANOMA-MEMBRANE COMPONENT AS A TOOL FOR DETECTING CIRCULATING ANTIBODIES.

Birkmayer GD
Institut fur Zellbiologie, Goethestrasse 33, D-8000 Munchen 2, W. Germany
Cancer; 48(11):2399-2408 1981

In search of tumor-associated components in human melanomas and gliomas, plasma membranes were isolated from these tumors and compared morphologically, biochemically and immunologically with those from normal human brain. The preparations exhibited a comparable ultrastructure of empty vesicles of various form and size. The melanoma membrane consisted of at least 15 protein components and the glioma membrane consisted of at least 24 protein components, 4 of which were absent in the membrane of normal tissue, as revealed by polyacrylamide gel electrophoresis. The four tumor-associated polypeptides could be solubilized together with a few other membrane components by the non-ionic detergent Triton-X100 and were used as an antigen source for immunologic characterization of melanoma and glioma membranes. A rabbit antiserum prepared against these solubilized membrane components from melanoma and glioma membranes. A rabbit antiserum prepared against these solubilized membrane components from melanoma was absorbed with plasma membranes from a variety of normal tissue including RBC, lymphocytes, spleen, liver, lung, kidney, placenta and brain. The absorbed antiserum reacted with the membrane extract of all the 11 melanomas tested so far; in addition it crossreacted with an identically prepared extract from all the 15 gliomas tested. Membrane extracts from other tumors, such as kidney and mammary carcinoma, were negative in this respect. Furthermore, a rabbit antiserum prepared against the Triton extract from glioma membranes yielded after exhaustive absorption an immune precipitate not only with the specimens from the 15 other gliomas but also with those from the 11 melanomas. Electrophoretic analysis of the immune precipitate formed by the Ig fraction of the absorbed rabbit antiserum and the Triton-X100 extract from melanoma membranes exhibited six polypeptide bands, two of which appear antigen-derived as they were missing in the profile of the Ig pattern. A comparable electrophoretic pattern was obtained with the immune precipitate of the glioma antigen specimen. The mol wt of these two polypeptide was estimated on the basis of their electrophoretic mobility to be 55,000 and 10,000 daltons, respectively. The electrophoretic immunologic findings argue for a common membrane component in human melanoma and glioma patients. Using the Triton extract from melanoma membranes as an antigen source, precipitating antibodies could be detected in the Ig fraction of 16 of the 24 sera from melanoma patients and in that of 15 of the 23 glioma patients by means of counter-current electrophoresis. Sera from a variety of cancer patients with diseases other than melanoma or glioma as well as from patients without cancer were negative in this respect. (Author abstract) (37 Refs)

12. HUMORAL AND CELLULAR REACTIONS TO PLACENTAL ANTIGENS IN WOMEN WITH PATHOLOGIC PREGNANCIES AND CANCER PATIENTS.

Corocleanu MN
County Hosp., Brasov, Romania
Rev Roum Biochim; 18(1):7-13 1981

The results of id reactions (IDR) with a placental suspension in 50 pregnant (normal or pathologic) and postpartum women and in 15 cancer patients (12 incipient clinical and 3 advanced) are presented. In 34% of these subjects the reaction was negative; these were either normal subjects (normal pregnancies in the last term or postpartum) or tumor carriers in an advanced stage. In women with pathologic pregnancies or in tumor carriers in incipient clinical states, the IDR was clearly positive. In another 30 patients, a comparative investigation was carried out by IDR to placental suspension and by precipitation reaction (IP) between crude and soluble placental antigen and the patients' sera. A good agreement of the IDR and IP was obtained; 90% of the patients showed similar results with both methods. Double diffusion of sera from women with pathologic pregnancies and tumor extracts gave positive results in 60% of the cases. The placental antigen which reacts in immunodiffusion with the serum of pregnant women or tumor carriers was characterized using physicochemical and immunochemical methods. The results of the analyses suggested that the placental antigen is an alpha-2-globulin with a mol wt of approx 40,000 daltons. By fluoroimmunoelectrophoresis, it was demonstrated that the antiplacental antibodies in the sera of women with pathologic pregnancy belonged to one of the three major immunoglobulin classes (IgG). (7 Refs)

TUMOR ANTIBODIES ASSOCIATED WITH VIRUSES

13. IDENTIFICATION OF ANTIGENIC DETERMINANTS UNIQUE TO THE SURFACES OF CELLS TRANSFORMED BY EPSTEIN-BARR VIRUS.

Kintner C, Sugden B
Div. Biology, California Inst. Technology, Pasadena, CA, 91125
Nature; 294(5840):458-460 1981

Four monoclonal antibodies (anti-EBVCS) that detect antigenic determinants uniqu e to the surfaces of Epstein-Barr virus (EBV)-transformed cells but are not associated with virus production were isolated. Cell lines transformed in vitro or those transformed in vivo but not associated with Burkitt's lymphoma bound anti-EBVCS strongly, whereas cell lines from patients with Burkitt's lymphoma bound them at intermediate levels or not at all. When untreated lymphocytes and lymphocytes exposed to EBV, Concanavalin A, and pokeweed mitogen were assayed, only EBV-exposed lymphocytes expressed EBVCS determinants, which were detectable within 48 hr after infection. Assay of unseparated populations of EBV-exposed primary lymphocytes and immunoglobulin-positive and -negative populations indicated that those cells which express EBVCS determinants are separated as B cells along with those which express the EBV-induced nuclear antigen and that the two antigen-expressing populations are overlapping and may be identical. A polypeptide with an apparent mol wt of 45,000 was precipitated from an EBVCS-positive cell line and was likely to be the molecule which carries EBVCS determinants. The results indicate that EBVCS determinants are expressed at reduced levels on cell lines established from Burkitt's lymphoma patients relative to expression on other EBV-transformed cell lines. EBVCS determinants are among possible determinants recognized by autochthonous, cytotoxic T cells specific for EBV-transformed cells and may therefore be equivalent to lymphocyte determined membrane antigen (LYDMA); this possibility was supported by the finding that EBVCS and LYDMA were expressed with the same time course in lymphocytes infected with EBV in vitro. If the EBVCS determinants are used by cytotoxic T cells to identify their targets, reduced expression of EBVCS on Burkitt's lymphoma cell lines is consistent with these tumor cells having been selected in vivo to survive that cytotoxic response. (18 Refs)

14. GENITAL CANCER AND VIRUSES.

Rapp F, Jenkins FJ
Dept. Microbiology, Pennsylvania State Univ. Coll. Medicine, Hershey, PA, 17033
Gynecol Oncol; 12(2,part2):S25-S41 1981

Current data suggesting an association between viruses and genital cancer are reviewed. The main emphasis is on the relationship between herpes simples virus Type 2 (HSV-2) and cervical cancer. Seroepidemiological studies are presented along with emphasis on HSV-transforming and oncogenic potential. Although the evidence is indirect, it is highly suggestive. HSV-2 has the oncogenic potential to produce neoplastic disease in animals. The ability of HSV-2 to transform cells in vitro and for transformed cells to produce tumors in vivo is presently the most direct evidence for oncogenic potential. In vivo experiments, more closely linking HSV-2 and cervical cancer are hampered by the severe cytopathic effect of HSV-2. Evidence associating two other viruses, human cytomegalovirus (CMV) and human papilloma virus (PV), with cervical and prostatic cancer are also discussed. Factors associating CMV with genital cancer include the establishment of persistent infections of the genitourinary tract, transmission by sexual contact, seroepidemiological studies with antibodies and genital cancer, detection of virus particles or virus-specific antigens in genital cancer biopsies, and in vitro transformation studies. Factors associating PV with genital cancer include association with venereal disease, conversion of condylomata acuminata to malignant state, and detection of genital carcinoma within condylomata. (97 Refs)

15. POSSIBLE ROLE OF HERPES VIRUS-2 IN ETIOLOGY OF CERVIX CARCINOMA.

Vasil'ev BV, Iovlev VI, Kniazev PG, Bokhman IaV, Smorodintsev AA
N. N. Petrov Res. Inst. Oncology, Leningrad, USSR
Akush Ginekol (Mosk); (9):20-22 1981

Complement fixation tests showed significant increases in titers of specific antibodies against herpes simplex virus-2 (HSV-2) in the blood sera of patients with cervix carcinoma, compared with sera of healthy controls. The number of patients with high titers of antibodies against HSV-2 was 1.5-3x greater than the number with high titers against HSV-1. These findings confirm the role of HSV-2 in the etiology of cervix carcinoma. (10 Refs) (In RUS)

16. ESTABLISHMENT AND CHARACTERIZATION OF PERMANENT CELL LINES FROM PATIENTS WITH ACUTE AND HAIRY CELL LEUKEMIA.

Stockbauer P, Cinatl J, Mach O
Inst. Hematology and Blood Transfusion, 128 20 Prague, Czechoslovakia
Neoplasma; 28(4):385-395 1981

Four cell lines were established from peripheral blood of patients with leukemia. All lines express the Epstein Barr virus nuclear antigen (EBNA) and therefore should be classified as lymphoblastoid cell lines. However, one of the lines UHKT-5 established from a patient with acute myelomonocytic leukemia has some features not typical for lymphoblastoid cell lines. The cells resemble macrophages with the phagocytic ability for yeasts, strong alpha-naphthylacetate esterase positivity in phagocytizing cells and unusually long villi. Another line UHKT-7 established from a patient with hairy cell leukemia expresses the same isotype of membrane Ig as the original hairy cells. (Author abstract) (26 Refs)

17. EFFECT OF THE AGE-RELATED IMMUNE DEPRESSION INDUCED BY MTV ON THE IN VIVO GROWTH OF A MAMMARY CARCINOMA.

Tagliabue A, Luini W, De Vito G, Boraschi D
Istituti di Ricerche Farmacologiche 'Mario Negri', Via Eritrea 62, 20157 Milan, Italy
Br J Cancer; 44(3):460-463 1981

The interactions between immune responses and mouse mammary tumor virus (MTV) were studied in C3H/HeN mice. MTV-infected and MTV-free mice were immunized with sheep RBC and the splenocytes were tested for their ability to produce antibodies against MTV. Significant depression of plaque-forming cells was observed in 14-20 wk old MTV-infected mice, compared with MTV-free mice of the same age. The immune response of 8 and 36 wk old MTV-infected mice was almost similar to that of age-matched MTV-free mice. Analysis of the in vivo growth of transplanted mammary gland carcinoma showed that median survival times and median latent periods in MTV-infected mice were shorter than those in MTV-free mice. (18 Refs)

18. A GEOGRAPHICAL STUDY OF ANTIBODIES TO MEMBRANE ANTIGENS OF HSV-2-INFECTED CELLS AND HSV-2-SPECIFIC ANTIBODIES IN PATIENTS WITH CERVICAL CANCER.

Mendis LN, Best JM, Senarath L, Chiphangwi J, Vestergaard BF, Banatvala JE
Dept. Microbiology, Faculty of Medicine, Post Office Box 271, Kynsey Road, Colombo 8, Sri Lanka
Int J Cancer; 28(5):535-542 1981

Sera were obtained from patients with squamous carcinoma of the cervix from Great Britain (29), Sri Lanka (32), Malawi (27) and Sudan (27), and from controls from all countries except Sudan. Controls were matched for ethnic origin, age and social class. Sera were tested by indirect immunofluorescence (IF) for IgG and IgA antibodies to membrane antigens (MA) and IgA antibodies to VCA of HSV-2 infected cells. Compared with controls, IgA antibodies to MA (IgA anti-MA) were detected more frequently and at higher titers in all groups of patients. However, there was no significant difference in prevalence of these antibodies at titers greater than or equal to 1:4 between Malawian patients and controls, although a significantly higher proportion of patients had IgA anti-MA titers of greater than or equal to 1:16. In contrast, IgA anti-VCA did not distinguish patients from controls. More than 90% of both patients and controls from all countries had IgG antibodies to MA (IgA anti-MA). Malawian patients had a significantly higher geometric mean titer (GMT) of IgG anti-MA than controls and both patients and controls had significantly higher GMTs than their counterparts from other countries. The variation between herpes IgG anti-MA titers in subjects from different countries did not reflect differences in serum Ig levels and similar variations in titer were not seen in rubella and measles HAI titers. Among the patients there was a geographical variation in the prevalence of HSV-2 specific antibodies detected by ELISA, which varied from 52% among British and Sudanese patients to 73% among Malawian patients. Even when adjustment was made for possible false negative results, there were between 10 and 31% patients without HSV-2-specific antibodies, although only 2 of 103 (1.9%) patients had neither HSV-1 nor HSV-2 antibodies. The association of HSV-2 with cervical carcinoma appeared to vary with age. (Author abstract) (52 Refs)

19. RETROVIRUS P30-RELATED ANTIGEN IN HUMAN SYNCYTIOTROPHOBLASTS AND IGG ANTIBODIES IN CORD-BLOOD SERA.

Suni J, Wahlstrom T, Vaheri A
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Int J Cancer; 28(5):559-566 1981

Sensitive immunological techniques were used to detect retrovirus markers in human pregnancy. A total of 1,540 human cord-blood sera were tested for retrovirus-reactive IgG antibodies using solid-phase enzyme immunoassay and purified RD114 virus as antigen. Of these, 118 (7.7%) sera were positive. Blocking assays with specific animal anti-p30 sera, use of control antigen, and electrophoretic protein experiments combined with immunological detection indicated that the human antibodies reacted specifically with the p30 protein. The occurrence of antibodies in cord-blood serum had a highly significant correlation to complications during pregnancy and also correlated to the number of previous absorptions and stillbirths. When goat anti-RD 114 p30 serum was used in the peroxidase-anti-peroxidase tissue staining procedure, p30-related antigen was detected in sections of all placental specimens (early and term pregnancies, blighted ova, hydatidiform moles, destructive moles and choriocarcinomas). However, in each case only syncytiotrophoblastic cells were positive. These findings, supplemented with different types of blocking tests, lead us to conclude that retrovirus p30-related antigen is selectively expressed in the highly differentiated syncytiotrophoblasts, which in the normal placenta are directly exposed to maternal blood. It is suggested that retrovirus-reactive antibodies may represent an autoimmune-like immune response to the p30-related syncytiotrophoblast antigen escaping during cellular damage. (Author abstract) (32 Refs)

20. ONCOGENIC ACTIVITY OF THE BK TYPE OF HUMAN PAPOVA VIRUS IN NEWBORN WISTAR RATS.

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Arch Virol; 69(3/4):239-251 1981

The oncogenic potential of the human papova virus BK (= BKV) has been examined in newborn Wistar rats. Twelve of 37 animals inoculated with BKV sc and 7 of 40 animals inoculated with BKV ic developed tumors of various histological types. The latency periods ranged from 6 to 18 mo. The BKV etiology of tumors was supported by detection of BKV T antigen in cells of established tumor lines by means of indirect immunofluorescence. No tumors appeared in animals given injections of saline instead of virus. BKV T antibodies were detected in sera of 100% of animals bearing tumors but not in sera of control animals. Only 3 of 77 BKV infected and none of the control animals developed spontaneous tumors (adenomas). (Author abstract) (16 Refs)

21. DYNAMICS OF EPSTEIN-BARR VIRUS ANTIBODIES IN HODGKIN'S DISEASE.

Vanecek K, Holy J, Hrodek O, Hynieova H, Ptrtylova K, Srajer J

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Cesk Pediatr; 36(8):449-452 1981

The dynamics of antibodies to Epstein-Barr Virus capsid antigen (VCA/EBV) was studied in 38 children (26 boys and 12 girls) with Hodgkin's disease (HD). The course of the disease was protracted with remissions and recurrences in 16 cases (Group A), short, with death in a short time in 5 (Group B), and 17 other patients (Group C) were in remission without recurrence for 3-5 yr after treatment. The treatment consisted of radiotherapy followed by single-agent or polychemotherapy with cyclophosphamide, vinblastine, prednisone, and procarbazine. The antibody titer correlated with the severity and course of the disease, dropping rapidly from a very low level in Group B, and rising from higher initial levels in Group A and especially C. The antibody titers were not affected by the treatment. (7 Refs) (In CZE)

ANTITUMOR ACTIVITY AND IMMUNOTHERAPY

22. MONOCLONAL ANTIBODIES RECOGNIZING NORMAL HUMAN T LYMPHOCYTES AND MALIGNANT HUMAN B LYMPHOCYTES: A COMPARATIVE STUDY.

Martin PJ, Hansen JA, Sladak AW, Nowinski RC
Fred Hutchinson Cancer Res. Center, Seattle, WA, 98104
J Immunol; 127(5):1920-1923 1981

We have undertaken a direct comparison of eight different murine monoclonal antibodies that recognize antigens shared by human T cells and certain malignant B cells. Immune precipitation, lysostripping, and competitive binding experiments indicate that the antigenic determinants detected by antibodies Leu 1, T101, 17F12, SC1, A50, OKT1, and 10.2 are closely associated on the same molecular species and may in fact be identical. The antigenic determinant recognized by antibody 12.1, which has properties similar to the one detected by other antibodies, is present on a distinct cell-surface molecule. Our results emphasize the importance of a quantitative direct comparison of different monoclonal antibodies in distinguishing newly reported antibodies from those already described. Such a comparison can resolve apparent discrepancies that arise either from methodologic variations or from differences in antibody avidity. (Author abstract) (21 Refs)

23. CELLULAR AND HUMORAL IMMUNITY IN HODGKIN'S DISEASE: I. PATIENTS IN CONTINUOUS LONG-TERM REMISSION.

Skovmann-Sorensen O, Schroder H, Moller-Larsen A, Haahr S
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Scand J Haematol; 27(3):171-180 1981

Cell-mediated and humoral immunity to herpes simplex virus (HSV), cytomegalovirus (CMV) and varicella zoster virus (VZV) were examined in 37 patients with Hodgkin's disease in continuous long term remission. This group had lower blast transformation than a matched control group to all three antigens. Patients originally showing B-symptoms had higher transformation to VZV than those with A-symptoms. Patients treated with irradiation only had higher transformation than those treated with either chemotherapy or a combination of chemotherapy and irradiation. There was a clear tendency towards lower transformation in patients having been in remission for 2 yr or less. Phytohemagglutinin (PHA) stimulation gave lower response in the patient group than in the control group. Patients with B-symptoms had lower response than those with A-symptoms. Interferon production was specially impaired in patients with B-symptoms. The patient group had higher CF titers against HSV and CMV while the control group had higher titers against VZV. B-symptom patients had higher titers against VZV than A-symptom patients. It is concluded that HD patients have impaired immune function many years after discontinuation of therapy, but there are certain differences regarding the in vitro immunity within the patient groups. (Author abstract) (17 Refs)

24. LEUKEMIC CELL TARGETING AND THERAPY BY MONOCLONAL ANTIBODY IN A MOUSE MODEL SYSTEM.

Scheinberg DA, Strand M
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Cancer Res; 42(1):44-49 1982

A monoclonal antibody prepared against the Rauscher virus envelope glycoprotein with a mol wt of 70,000 was targeted to neoplastic cells and cured the Rauscher leukemia virus-induced erythroleukemia in BALB/c mice. This antibody, 103A, specifically reacted with the Rauscher and Friend erythroleukemia viruses and erythroleukemic cells but did not react with other murine ecotropic or xenotropic viruses or feline leukemia virus or with normal spleen cells, thymocytes, or fibroblasts, as measured by radioimmunoassays. P3, a control antibody of the same Ig G1 subclass, did not bind to any of these cells or viruses. This specificity was maintained in vivo. 125I-Labeled 103A injected into mice targeted to leukemic spleen cells but not to normal cells. Mean uptake ratios of binding to leukemic over normal spleen cells ranged from greater than 70 at 7 hr after injection to less than 10 at 40 hr later. The control antibody showed no binding in vivo. A single small dose of 103A was able to cure leukemic mice as assayed by spleen focus formation on Day 8 or splenomegaly on Day 20. The 50% effective dose was 1.5 ug when injected 72 hr after onset of leukemia. The therapeutic potencies of drugs, toxins, and cytotoxic radioisotopes conjugated to antibodies can be quantitatively compared using the established dose-response curve. Such quantitative comparisons showed that 131-labeled 103A Ig G was no more potent than unlabeled 103A Ig G in this system . (Author abstract) (39 Refs)

25. EXPRESSION OF HUMAN FETAL BRAIN ANTIGENS BY HUMAN TUMORS OF NEUROECTODERMAL ORIGIN AS DEFINED BY MONOCLONAL ANTIBODIES.

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Cancer Res; 42(1):267-275 1982

The antigenic relationships between human tumors of neuroectodermal origin and fetal brain were investigated by the production of hybridoma antibodies derived from a fusion of P3-NS1/1-Ag 4-1 (NS1) myeloma cells with splenocytes from a mouse multiply immunized with a homogenate of second-trimester human fetal brain tissue. Two monoclonal antibodies (MAs), 4D2cl 6 and 7H10cl 4, were studied in detail by cell surface radioimmunoassay (CS-RIA), quantitative absorption, indirect immunofluorescence, and peroxidase-anti-peroxidase (PAP) immunohistology. MA 4D2cl 6 binds to 5 of 14 glioblastoma (GBM) cell lines, 1 of 2 melanoma cell lines, 1 of 3 neuroblastoma cell lines, and 1 of 5 fetal fibroblast lines by CS-RIA and to 13 of 13 GBM, 1 neuroblastoma, and fetal brain, liver, spleen, and adult spleen unfixed frozen tissue by PAP analysis. MA 7H10cl 4 binds to 13 of 14 GBM, 1 of 3 neuroblastoma, and 1 medulloblastoma cell line(s) by CS-RIA analysis and to 13 of 13 GBM, 1 neuroblastoma, fetal brain, liver, spleen, thymus, and adult spleen by PAP analysis. Control non-CNS tumors and normal adult tissue, including brain, were unreactive with both MAs by CS-RIA, PAP, and absorption analysis. Tissue distribution and localization analyses established that MAs 4D2cl 6 and 7H10cl 4 recognize specificities of shared fetal-neuroectodermal-lymphoid distribution which are operationally specific within the adult CNS and which are not related to previously described oncofetal or onconeural antigens. (Author abstract) (36 Refs)

26. COMPLEMENT-DEPENDENT IN VITRO CYTOTOXICITY AGAINST AUTOLOGOUS INVASIVE BLADDER TUMOR CELLS IN HUMANS. EVALUATION OF THE POSSIBLE ROLE OF NATURALLY-OCCURRING ANTIBODIES IN COMPLEMENT-DEPENDENT CYTOTOXICITY.

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Acta Pathol Microbiol Scand [C]; 89(4):297-302 1981

Complement-dependent serum-mediated cytotoxicity (CDC) was measured in a 51-chromium release assay against autologous tumor cells from seven non-invasive and nine invasive transitional-cell tumors of the urinary bladder. CDC was demonstrated against tumor cells from invasive tumors. Heat-inactivation of autologous sera lead to complete loss of cytotoxicity. There were no differences in CDC of autologous sera from patients and allogenic sera from controls. The cytotoxic response seems to be strongly dependent on the target cell. CDC was significantly reduced by use of an allogenic C 2 deficient serum. Direct immunofluorescence did not reveal any tumor cell associated Ig of IgG or IgM classes. Indirect immunofluorescence with autologous heat-inactivated sera demonstrated in most cases both IgG and IgM attachment to the tumor cells, but there were no obvious relations between indirect immunofluorescence and CDC. Absorption of allogenic sera to trypsin- or neuraminidase-treated RBC did not affect CDC of these sera against invasive tumor targets. The results indicate a complement-dependent cytotoxicity against target cells from invasive bladder tumors. Complement seems to be activated through the classical pathway, but the possible role of naturally-occurring antibodies against invasive tumor targets is not clarified. (Author abstract) (17 Refs)

27. IMMUNOLOGICAL STUDIES IN CHRONIC LYMPHOCYTIC LEUKEMIA. I. ELUCIDATION OF SUBSET HETEROGENEITY.

Hokland P, Ellegaard J
Med. afd. II, Aarhus Amtssygehus, 8000 Aarhus C, Denmark
Leuk Res; 5(4/5):341-348 1981

The B lymphocyte subsets in chronic lymphocytic leukemia (CLL) were examined by three different approaches: rosette sedimentations, double marker assays, and separation of CLL cells according to their densities in continuous Percoll gradients. A hypothesis of sequential alterations of the surface receptor in CLL is presented. RBC and mouse rosette tests yielded complementary results when 30 untreated CLL patients (43-81 yr old) were compared with 10 normal donors. The most stable marker of the malignant B cells was their ability to form rosettes with mouse RBC, while surface membrane immunoglobulins, IgG constant fragment-, and complement receptors were present only on a minor proportion of CLL cells. Lymphocytes forming rosettes with S-aminoethyl-iso-thiouronium bromide-treated sheep RBC were separated from non-rosette forming cells in eight patients; a very high percent of T cells were active RBC-rosette formers. When cells harvested from the non-T fractions were tested for mouse rosette formation, it was found that mouse rosette separation procedures are not as effective as those using sheep RBC: 22% of the cells harvested from the second interface were still able to form mouse rosettes. Double markers were found in 5/5 untreated patients. The surface marker phenotype of large cells, which are frequently seen in CLL patients, was determined. The results indicated considerable heterogeneity in CLL lymphocyte subsets. (25 Refs)

28. IMMUNOLOGICAL STUDIES IN CHRONIC LYMPHOCYTIC LEUKEMIA. II. NATURAL KILLER- AND ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY POTENTIALS OF MALIGNANT AND NON-MALIGNANT LYMPHOCYTE SUBSETS AND THE EFFECT OF ALPHA-INTERFERON.

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Med. afd. II, Aarhus Amtssygehus, 8000 Aarhus C, Denmark
Leuk Res; 5(4/5):349-355 1981

The effector cell potential of chronic lymphocytic leukemia (CLL) subsets was determined in the natural killer (NK) and antibody-dependent cellular cytotoxicity (ADCC) assays. Lymphocyte subpopulations were isolated from peripheral blood obtained from 25 (43-76 yr old) CLL patients. The behavior of CLL cells in NK and ADCC assays was determined. Basic experimental conditions for the assays were determined. When unseparated lymphocytes from CLL patients were tested in NK (21 patients) and ADCC (25 patients) assays and compared to the cytotoxicities of 20 normal donors, the CLL cells were defective in both tests. The behavior of CLL cells in NK assays was defective with or without 1,000 IU alpha-interferon (AIF). The NK and ADCC defects were found mainly in the non-T fraction, while the T cells exhibited subnormal levels of lysis. By depleting the non-T cells of mouse rosette forming cells, a null cell subset was purified that exhibited considerable lysis in the NK test. AIF did not enhance ADCC by unfractionated CLL cells. When the NK activity of three CLL patients were tested against 7 target cell lines with NK sensitivities in normal donors ranging from very low to extremely, the same pattern was retained in the patients, although the addition of AIF tended to diminish the tendency by boosting the NK activity against the resistant lines proportionately more than against the sensitive ones. Compared with lysis by cells from normal donors, the lysis of cells from the patients, was still defective with all cell lines tested. (19 Refs)

29. REACTIVITY OF A MONOCLONAL ANTIBODY WITH HUMAN OVARIAN CARCINOMA.

Bast RC, Feeney M, Lazarus H, Nadler LM, Calvin RB, Knapp RC
Sidney Farber Cancer Inst., Boston, MA, 02115
J Clin Invest; 68(5):1331-1337 1981

A murine monoclonal antibody (OC125) has been developed that reacts with each of six epithelial ovarian carcinoma cell lines and with cryopreserved tumor tissue from 12 of 20 ovarian cancer patients. By contrast, the antibody does not bind to a variety of nonmalignant tissues, including adult and fetal ovary. OC125 reacts with only 1 of 14 cell lines derived from nonovarian neoplasms and has failed to react with cryostat sections from 12 nonovarian carcinomas. (Author abstract) (43 Refs)

30. ANTIBODY DIRECTED AT A SURFACE STRUCTURE INHIBITS CYTOLYTIC BUT NOT SUPPRESSOR FUNCTION OF HUMAN T LYMPHOCYTES.

Reinherz EL, Hussey RE, Fitzgerald K, Snow P, Terhorst C, Schlossman SF
Div. Tumor Immunology, Dept. Medicine, Sidney Farber Cancer Inst., Harvard Medical Sch., 44 Binney St., Boston, MA, 02115
Nature; 293(5837):168-170 1981

The effect on T-cell function of three monoclonal antibodies reactive with the cytotoxic/suppressor subset was studied. Anti-T8A antibody markedly inhibited cell mediated lympholysis (approx 0.7-2.0% specific lysis compared with approx 21-29% for controls), anti-T8 was partially inhibitory (approx 15-16%), and anti-T5 had no effect (approx 22-30%). None of the antibodies inhibited suppressor T-cell function in T- and B- cell interactions. The ability of one monoclonal antibody to inhibit binding by a second was determined by direct immunofluorescence. Results of these studies suggest that the determinant defined by anti-T5 is distinct from that defined by anti-T8A; anti-T8 and anti-T8A seem to react with a related structure. The molecular nature of these antigens was studied by polyacrylamide gel electrophoresis. Anti-T8 and anti-T8A precipitated molecules of the same mol wt. Although the antigens appear similar, and in sequential precipitation studies anti-T8A largely removed both the T8A and T8 antigens, anti-5 did not deplete T8 antigen. The results suggest that the T5 and T8 antigens are not identical. Both biochemical data and binding studies are consistent with the view that the T8 and T8A epitopes are located close together on a single molecule. Inhibition of cytotoxic cell function implies that the epitope defined by anti-T8A may be critical for cytolytic function but not for suppressor function. (19 Refs)

31. ACCELERATED APPEARANCE OF AN ASCITIC TUMOUR AFTER LONG-TERM APPLICATION OF INTERFERON TO NZB/W MICE.

Borecky L, Lackovic V, Clampor F, Rovensky J, Ujhazy V, Matoska J, Svec J, Poverennyi AM
Inst. Virology, Slovak Academy Sciences, 809 39 Bratislava, USSR
Acta Virol (Praha); 25(5):283-294 1981

In two similarly designed experiments female NZB/W mice treated with mouse L-cell interferon developed an ascitic tumor when the treatment was begun at 3.5 mo of age. But no tumor appeared within a 6 mo observation period when 6 mo old mice were used. A transient rise of anti-DNA antibodies preceded the tumor appearance in mice. The ascitic tumor was sensitive to antimetabolites and insensitive, or marginally sensitive, to alkylating agents or interferon. The tumor cells were adapted to growth in suspension in vitro. They caused tumor growth in various inbred and random-bred mouse lines. Attempts to transfer the tumor to Swiss mice with cell-free preparations were unsuccessful. (Author abstract) (22 Refs)

32. IN VIVO TUMOR LOCALIZATION USING TUMOR-SPECIFIC MONKEY XENOANTIBODY, ALLOANTIBODY, AND MURINE MONOCLONAL XENOANTIBODY.

Stuhlmiller GM, Sullivan DC, Vervaert CE, Croker BP, Harris CC, Siegler HF
Duke Univ. Medical Center, Box 3917, Durham, NC, 27710
Ann Surg; 194(5):592-601 1981

Specific in vivo localization of antibodies reactive with human melanoma cell membrane tumor associated antigens (TAA) has been attempted using congenitally athymic nude mice bearing sc human melanoma tumor xenografts as the experimental model. IgG fractions were prepared from each of several immune and control sera. Antimelanoma antibody sources included human alloantibody obtained from melanoma patients immunized against allogeneic melanoma cells, a monkey antiserum raised by immunization against a single human melanoma cell line, and a murine monoclonal antimelanoma antibody-secreting hybridoma cell line. Localization of these radiolabeled antibodies and of control IgG preparations to tumor tissue was determined by whole body scintigraphy and by differential tissue counting. Compared with the different control IgG preparations, each of the antimelanoma IgG preparations exhibited significant specific accumulation within the melanoma tissue. However, variation existed in the ability of each antimelanoma IgG to tumor preparation to localize despite attempts to control model parameters such as tumor source, in vivo passage number and mass. This variation appears to reflect basic biologic differences between tumors in different animals and possibly differences in the antigen-binding capacities of each IgG preparation following radioiodination. This technique for tumor localization is very promising and has obvious potential for clinical application. (Author abstract) (16 Refs)

33. EXPLOITATION OF MONOCLONAL ANTIBODIES: A 'WHO'S WHO' OF HAEMOPOIETIC MALIGNANCY.

Greaves MF, Delia D, Robinson J, Sutherland R, Newman R, Moore MA, Lajtha L, Gallo R, McCulloch EA, Boggs D, Sachs L
Imperial Cancer Res. Fund Laboratories, POB 123, Lincoln's Inn Fields, London WC2A 3PX, England
Blood Cells; 7(2):257-280 1981

A panel of monoclonal antibodies plus other conventional markers (such as anti-terminal deoxynucleotidyl transferase) were used to explore detailed phenotypes of leukemic cells in relation to normal hemopoietic differentiation. Consistent, composite phenotypes of different subclasses of lymphoid malignancies closely mimic those of corresponding normal cells at equivalent stages of differentiation. The study indicates three major target cell populations are available for lymphoid malignancy: the pluripotential stem cell; lymphoid progenitors or stem cells in bone marrow; and long-lived, mature and immunocompetent T and B cells. The major phenotypes in different leukemias represent the level of 'maturation arrest' imposed on the dominant subclone; this is determined by, but not necessarily synonymous with, the 'target cell' and associated clonogenic cell population in the leukemia. No consistent major abnormalities of gene expression were found; while such may exist, it is suggested that they are irrelevant to the central issue of what alterations are essential and sufficient for the evolution of clonogenic leukemic cells. It is proposed instead that subtle changes, which uncouple proliferation and differentiation, are all that is required. (77 Refs)

34. STUDIES ON T CELL BEARING FC RECEPTORS FOR IGG OF PERIPHERAL LYMPHOCYTES IN PATIENTS WITH BLADDER CARCINOMA.

Shimatani N
Dept. Urology, Kobe Univ. Sch. Medicine, Kobe, Japan
Hinyokika Kiyo; 27(6):537-647 1981

To test the cellular immunocompetence in patients with bladder carcinoma, a study was made on the lymphocyte subpopulation of 34 patients and 35 healthy men. T cell was identified by spontaneous rosette formation with sheep RBC, and B cell was identified by EAC rosette formation. T lymphocytes bearing Fc receptors for IgG (IgGFcR+ T cells) were detected by double rosette formation of neuraminidase treated sheep

RBC and glutaraldehyde treated sensitized ox RBC. The percentages of IgGFcR+ T cells in total T cells in peripheral lymphocytes of 35 healthy men and 34 untreated bladder cancer patients were 5.8 +-1.9% and 14.2 +-8.4% respectively, the percentages of T cells in peripheral lymphocytes of 35 healthy men and 34 untreated bladder cancer patients were 81.3 +-6.3% and 68.6 +-14.0% respectively. The difference between these figures was statistically significant. There was a tendency to decrease in percentage and absolute count of T cells in the patients with higher grade and stage of the tumor. Contrary, there was a tendency to increase percentages of IgGFcR+ T cells in total T cells of the patients with higher grade and stage of the tumor. No influence of operation was found on T cell percentage, absolute count of T cell and the percentage of IgGFcR+ T cells in total T cells. Steroids which were secreted by stimulation of operative stress might have an effect on the percentages of IgGFcR+ T cells in total T cells. (Author abstract) (33 Refs) (In JPN)

35. STUDIES ON NATURAL KILLER (NK) CELLS. II. SEROLOGIC EVIDENCE FOR HETEROGENEITY OF MURINE NK CELLS.

Burton RC, Bartlett SP, Kumar V, Winn HJ
Transplantation Unit, General Surgical Services, Harvard Medical Sch. Massachusetts General Hosp., Boston, MA, 02114
J Immunol; 127(5):1864-1868 1981

NK cells are divided into two subclasses on the basis of cell surface antigens: NKA cells, which preferentially lyse lymphoma cells and which are readily destroyed by treatment with anti-H-2, rabbit anti-mouse, or anti-NK specific antibodies in the presence of C; and NKB cells, which preferentially lyse nonlymphoma tumor cells and which are resistant to anti-NK specific antibodies, partially sensitive to anti-H-2 specific antibodies, and only fully sensitive to rabbit anti-mouse serum and C. Thus, suspensions of spleen cells that were treated with anti-NK-1.2 antibodies and C lost virtually all lytic activity for six lymphoma cell lines, whereas lytic activity for two nonlymphoma cell lines remained largely intact. It must be noted, however, that unlike NK-1.2 expression, target cell preference is not an absolute indicator of NK cell subclass. Cytotoxic T cells were readily distinguished from NKA and NKB cells on the basis of their sensitivity to monoclonal anti-Thy1.2 antibodies and resistance to anti-NK-1.2 a ntiserum and C. (Author abstract) (23 Refs)

IMMUNOGLOBULIN STRUCTURE AND SYNTHESIS

36. IMMUNOGLOBULIN HEAVY CHAIN GENES IN HUMANS ARE LOCATED IN CHROMOSOME 14.

Hobart MJ, Rabbitts TH, Goodfellow PN, Solomon E, Chambers S, Spurr N, Povey S
MRC Mechanisms in Tumour Immunity Unit, MRC Centre, Hills Road, Cambridge CB2 2QH, England
Ann Hum Genet; 45(4):331-335 1981

Human chromosomes were segregated by developing mouse-human somatic cell hybrids. DNA from these hybrids was cleaved by restriction endonucleases and assessed for presence of human immunoglobulin heavy chain constant and variable region genes. The heavy chain gene complex was located on chromosome 14. (20 Refs)

37. DEVELOPMENTAL HIERARCHY OF IMMUNOGLOBULIN GENE REARRANGEMENTS IN HUMAN LEUKEMIC PRE-B CELLS.

Korsmeyer SJ, Hieter PA, Ravetch JV, Poplack DG, Waldmann TA, Leder P
Metabolism Branch, NCI, NIH, Bethesda, MD, 20205
Proc Natl Acad Sci USA; 78(11,part2):7096-7100 1981

We have used a special class of human acute lymphocytic leukemias, the common 'non-T/non-B' cell type, to define a hierarchy of genetic rearrangements that occur during the earliest stages of B-cell maturation. This has allowed us to identify intermediate cells predicted by a hierarchial model in which Ig heavy chain variable region gene formation precedes that of light chain and in which kappa light chain gene formation precedes that of lambda. The model emphasizes the flexible nature of Ig gene recombination that not infrequently produces aberrant or null genes that are phenotypically excluded from expression. Remaining alleles or isotypic genes can then be utilized as 'spares' undergoing recombination until a valid gene is formed. Significantly, the excluded allele or isotype is frequently deleted from the genome. In addition to defining a pathway of genetic maturation, this analysis provides a powerful means to further classify cases of non-T/non-B-cell acute lymphocytic leukemia, most of which seem to reside at early stages along the B-cell pathway of differentiation. (Author abstract) (44 Refs)

38. MAPPING OF IMMUNOGLOBULIN VARIABLE REGION GENES: RELATIONSHIP TO THE 'DELETION' MODEL OF IMMUNOGLOBULIN GENE REARRANGEMENT.

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Dept. Microbiology and Immunology, SC-42, Univ. Washington, Seattle, WA, 98195
Nucleic Acids Res; 9(21):5725-5735 1981

Five families of variable region genes of mouse kappa chains were analyzed by Southern blot hybridization to determine their relative chromosomal map positions. Map positions were deduced by Vkappa gene deletion from antibody-producing cells expressing upstream Vkappa genes and retention in cells expressing downstream genes. The Vkappa regions expressed in the myelomas MOPC167, MPC11, MOPC21 and ABPC20 are members of Vkappa families exhibiting one, three, six and six major germline hybridization bands respectively. The gene order of the five families in germline DNA was found to be VM167-VM11-(VM21, VA20) - VABE8-Jkappa - Ckappa. As expected in a deletion model of Ig gene rearrangement, a sequence located just 5' of J1 in germline DNA was found to be absent from some antibody producing cells which had not retained any germline Ckappa genes. However, other cell lines contained this sequence in rearranged contexts, suggesting that any deletion model of Ig V-J joining, as well as V gene mapping, must take into account the possibilities of stepwise rearrangements and reintegration of 'deleted' DNA. (Author abstract) (17 Refs)

39. ASSIGNMENT OF THE GENES FOR HUMAN LAMBDA IMMUNOGLOBULIN CHAINS TO CHROMOSOME 22.

Erikson J, Martinis J, Croce CM
Wistar Inst. Anatomy and Biology, 36th and Spruce St., Philadelphia, PA, 19104
Nature; 293(5837):173-175 1981

Somatic cell hybrids between mouse myeloma cells and either human peripheral lymphocytes or different human lambda chain-secreting lymphoblastoid cell lines were studied. Mouse x human hybridomas were pre-selected for the expression of human lambda chains; it was determined that only human chromosomes 14 and 22 were likely to carry the human lambda heavy-chain genes. To exclude the possibility that the human lambda-chain genes were located on chromosome 14 and confirm their assignment to chromosome 22, five independent lambda chain-secreting clones were subcloned and studied for expression of human lambda chains and isozyme markers assigned to each of the different human chromosomes. Chromosome 14 was excluded from consideration: two subclones lost chromosome 14 yet retained the ability to produce lambda chains. Results confirmed that the genes for lambda chains were on chromosome 22; the chromosome was the only human chromosome consistently present in all subclones secreting human lambda chains. Loss of human chromosome 22 resulted in loss of the ability to produce human lambda chains. (18 Refs)

40. INTERFERON ACTS DIRECTLY ON HUMAN B LYMPHOCYTES TO MODULATE IMMUNOGLOBULIN SYNTHESIS.

Harfast B, Huddlestone JR, Casali P, Merigan TC, Oldstone MB
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J Immunol; 127(5):2146-2150 1981

At different times of exposure, interferon (IFN) enhanced and suppressed pokeweed mitogen (PWM) induced IgG synthesis by human peripheral blood lymphocytes (PBL). Pretreatment of PBL with IFN frequently increased antibody production by more than 100% when compared with that by untreated PBL. Results of experiments in which PBL were separated into T and B subpopulations indicated that IFN preparations acted directly on B cells. Thus, mixtures of IFN-treated B cells and untreated T cells from five of seven persons tested produced 81% to 500% more IgG than untreated, matched control cells. However, IFN-treated monocytes mixed with untreated B and T cells or IFN-treated T cells mixed with untreated B cells failed to enhance IgG production significantly in similar assays. In contrast to the pretreatment protocol, when IFN was present in the incubation mixture throughout the PWM assay, IgG production decreased. Sephadex chromatography of the IFN and tests of the resulting fractions indicated that the IgG production-enhancing activity was located in the fraction carrying the antiviral activity. (Author abstract) (33 Refs)

41. IMMUNOGLOBULIN GLYCOPEPTIDES FROM AN IGG2B-PRODUCING MOUSE MYELOMA CELL LINE AND FROM VARIANT CELL LINES.

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Dept. Microbiology, State Univ. New York at Stony Brook, 20 Seward Lane, Stony Brook, NY, 11790
J Immunol; 127(5):2095-2101 1981

A mouse myeloma cell line, 45.6.3, produces an IgG2b Ig with two carbohydrate attachment sites on the heavy chains. One site is in the CH2 domain and the other in the VH region. The oligosaccharides at each site have different structures. The ratio of radioactive glucosamine incorporated in the VH compared with the CH2 oligosaccharide is approx 1:3. In an attempt to understand this observation further, variant cell lines derived from 45.6.3 were isolated and their Ig were characterized. A ricin-resistant line, R4R1.5, has the same two attachment sites as the wild type, but the ratio of radioactive glucosamine in VH compared with CH2 was 1:1 and not 1:3 as in the wild type. This alteration is most probably due to cellular factors, since the Ig protein is unchanged. The M3.11 cell line produces an Ig with a polypeptide deletion involving the CH3 domain. In this Ig, a third carbohydrate attachment site can be demonstrated. The percentage of radioactivity glucosamine in the CH2 domain compared with the total Ig is about 25% instead of 75% as in the wild type. These results suggest that the extent of glycosylation of different sites on Ig can be affected by both cellular factors and structural changes in the Ig protein. (Author abstract) (20 Refs)

HUMORAL IMMUNE BLOCKING FACTORS AND ANTIGEN-ANTIBODY COMPLEXES

42. ISOLATION OF LUNG CARCINOMA-ASSOCIATED ANTIBODIES FROM IMMUNE COMPLEXES AND PRODUCTION OF HETEROLOGOUS ANTISERA.

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Cancer Res; 42(1):292-300 1982

Immune complexes isolated from pleural effusions of lung carcinomas were dissociated by ion exchange chromatography in the presence of 8 M urea. The antibodies thus obtained from two lung adenocarcinomas and two squamous cell carcinomas were assayed by indirect immunofluorescence against a variety of target cells in fresh suspensions, tissue cultures, and paraffin-embedded sections. Strong cytoplasmic fluorescence was obtained with greater than 90% of the cell populations of all major histological types of lung carcinomas, and negative fluorescence was obtained with the cells of normal lung tissues and most of the nonpulmonary carcinomas. Antigen fractions prepared from the same lung carcinoma-associated immune complexes were used to immunize rabbits for the production of antisera directed against human lung carcinoma. The rabbit antibody preparations after proper absorptions were assayed in indirect immunofluorescence showing patterns of reactivity with normal and tumor cells of various derivations similar to those obtained with the human antibodies. Complete blocking of immunofluorescence staining with both allogeneic and xenogeneic antibody preparations was achieved by prior absorption with lung tumor tissue extracts or with various lung tumor antigen preparations. The present study demonstrates the isolation from lung tumor effusion immune complexes of antibodies with high affinity for lung carcinoma cells and of antigens that can be used to produce tumor-directed heterologous antibodies. The immunofluorescence staining of lung carcinoma-associated antigens in situ on paraffin-embedded sections provides new, topographical information. (Author abstract) (43 Refs)

43. EVALUATION OF DIFFERENT METHODS FOR DETECTING CIRCULATING IMMUNE COMPLEXES. STUDIES IN PATIENTS WITH LUNG CANCER.

Fust G, Fekete B, Angyal I, Jakab A, Pal A, Meretey K, Falus A, Torok K, Szegedi G, Kavai M, Puskas E, Csecsi-Nagy M, Szabo T, Lenkey A, Misz M
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J Immunol Methods; 46(3):259-276 1981

In a collaborative study involving 7 laboratories, sera from 53 patients with lung cancer, 37 primary and 16 secondary tumors, and sera of 40 healthy blood donors were tested by 19 different assays or assay modifications used for detecting immune complexes. In 12 out of 19 assays, significantly higher immune complex levels were found in the cancer patients than in the healthy subjects. Assays based on interactions between immune complexes and Fc receptors of different cells (lymphocytes, macrophages or platelets) discriminated between cancer patients and healthy subjects and a high percentage (47-87%) of positivity was observed in such assays in patients with lung cancer. In contrast, none of the tests based on immune complex-complement interactions discriminated between cancer patients and healthy subjects. Immunochemical analyses of the PEG precipitates obtained from the sera tested revealed that the concentrations of IgG, IgA and C3 were significantly higher in the precipitates obtained from patients' sera than from control sera, but no significant differences were seen in IgM and C1q concentrations. A 100% correct classification of individuals tested was obtained on discriminant analysis of results with 3 assays: EA rosette inhibition, ADCC inhibition and C3 concentration in PEG precipitates. Correlation between results obtained with individual sera by the different assays was very poor: significant correlation coefficients were found in only 13% of all possible paired comparisons. Our results suggest that Fc receptor-dependent assays are more suitable for detection and measurement of circulating immune complexes in lung cancer than tests based on interactions with complement. (Author abstract) (31 Refs)

44. IMMUNE COMPLEXES AND CANCER - UNMASKING THE HIDDEN HUMORAL IMMUNE RESPONSE TO NEOPLASTIC TISSUE.

Rossen RD
Dept. Developmental Therapeutics, Univ. Texas M. D. Anderson Hosp. and Tumor Inst., Houston, TX
Cancer Bull; 33(5):221-226 1981

A paradox seen in cancer is that plasma from tumor-bearing individuals, even when it contains antitumor antibody, may facilitate tumor growth. Methods of detecting soluble immune complexes (SIC) in sera and other body fluids, and their composition in cancer, are discussed. Biologic effects of CIS are discussed as well as circulating immune complexes and the mononuclear phagocyte system. CIS may have profound effects on cells such as suppression of of recruitment of new antigen-reactive lymphocytes and interference with Fc receptor function of mononuclear lymphoid cells. A prime reason to differentiate whether SIC in sera contain tumor-associated antigens or anti-idiotypes is to improve understanding of how immune complex formation influences regulation of host response to tumors. Operating on the assumption that CIS may be detrimental, attempts at their removal has resulted in claims of benefit in treatment of cancer. Unblocking of hidden tumor-specific cytotoxins also may be a major effect of therapy designed to remove soluble complexes from plasma. Very little is known about the composition and effects of SIC in patients with malignant diseases. (24 Refs)

45. SIGNIFICANCE OF SERUM IMMUNE COMPLEX ASSAY IN CANCER OF THE STOMACH AND COLON.

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Rinsho Meneki; 13(Suppl2):100-108 1981

This study represents an attempt to measure the circulating immune complexes in patents with cancer of the stomach or large intestine by the erythrocyte-amboceptor (EA) rosette inhibition test. The serum immune complex level determined by this method showed a significant correlation with that measured by the binding to surface receptors of cultured lymphoblasts (Raji cells) and a significant inverse correlation with the serum complement level (CH50). It did not correlate with the phytohemagglutinin skin test or lymphocytic blastogenesis assay, whereas the IgG.FcR+ T cell percentage was low in patients showing a high serum level of immune complexes. Clinically, circulating immune complexes were demonstrated in 66.7% of untreated patients with gastric carcinoma and 82.5% of those with carcinoma of the colon, in contrast with 5.9% in normal controls. Of these patients, those who received a curative operation and those who underwent immunochemotherapy and/or local continuous ia infusion with anticancer drugs displayed a significant decrease in circulating immune complexes. The results indicate that serum immune complexes can be measured by the EA rosette inhibition test; that there appears to be no correlation between the serum immune complex level and nonspecific cellular immune responsiveness; and that the IgG.FcR+ T cell percentage is not correlated with the serum concentration of the immune complexes but the data obtained suggest the presence of immune complexes attached to IgG.FcR+ T cells. (26 Refs) (In JPN)

46. PREGNANCY-ASSOCIATED BETA1-MACROGLOBULIN (BETA1-PAM): A NEW SERUM PROTEIN ASSOCIATED WITH PREGNANCY SERUM-DERIVED IMMUNE COMPLEXES AND OVARIAN CANCER.

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J Clin Lab Immunol; 6(2):141-145 1981

A new pregnancy-associated serum protein was found associated with pregnancy serum-derived immune complexes (IC). This protein was partially characterized and shown to be present in the blood of a majority of ovarian cancer patients. IC were obtained from late pregnancy serum and separated into their fractions. An antigen (mol wt range 4-5 x 10(5)) was identified which would consistently recombine with the IgG fraction from dissociated IC. Antisera were raised against the gel chromatographic fraction containing the putative IC component and following exhaustive absorption, were found to be specific for a serum protein with beta1-globulin electrophoretic mobility; this was termed pregnancy-associated beta1-macroglobulin (beta1-PAM). When beta1-PAM levels were estimated in the blood of various groups of subjects, comparatively high concentrations were found in a large proportion of ovarian cancer patients. Late pregnancy sera (40%) were also positive for beta1-PAM, but mostly at levels lower than those found in ovarian cancer, while the serum protein was only detected in 3/186 normal women and 1/62 patients with cervical cancer. Healthy males and subjects with cancer of the breast, colon, and testis were all negative for beta1-PAM. Beta1-PAM preparation obtained from both pregnancy and ovarian cancer sera were found to have the same ammonium sulfate precipitation range and isoelectric point. These data suggested that both beta1-PAM preparations are identical although mol wt values indicate some anomalies. (17 Refs)

47. ANTI-TRANSFERRIN RECEPTOR MONOCLONAL ANTIBODY AND TOXIN-ANTIBODY CONJUGATES AFFECT GROWTH OF HUMAN TUMOUR CELLS.

Trowbridge IS, Domingo DL
Dept. Cancer Biology, Salk Inst. Biological Studies, PO Box 85800, San Diego, CA, 92138
Nature; 293(5837):171-173 1981

The anti-transferrin receptor antibody-ricin A (A-RA) conjugate inhibits protein synthesis in a human T leukemic cell line (CCRF-CEM) almost as effectively as the intact ricin toxin. Antibody or ricin A subunit added alone or as a mixture inhibited protein synthesis only at concentrations 200-1,000x higher than the A-RA conjugate. The specificity of the A-RA conjugate is further indicated by the fact that protein synthesis in the mouse lymphoma cell line BW5147 was not inhibited by the anti-human transferrin receptor A-RA conjugate even though the cells were as sensitive as CCRF-CEM cells to the intact ricin toxin. Specific inhibition of protein synthesis in CCRF-CEM cells was also obtained with an anti-receptor antibody diphtheria fragment A conjugate. In vivo studies showed that the A-RA conjugate (50 ug iv, on days 0, 7, and 14) completely inhibited the growth of M21 cells in nude mice. However, a single iv injection of 880 ug unmodified anti-transferrin receptor antibody alone also inhibited sc melanoma cells. Antibody given 7 days after the inoculation of M21 tumor cells inhibited tumor growth as well. The unmodified antibody was much less effective in inhibiting HeLa cell growth in nude mice even after repeated doses. Further study of the therapeutic usefulness of anti-receptor antibodies is suggested. (31 Refs)

48. IMMUNODEFICIENCIES IN HODGKIN'S DISEASE. PART I: T CELL-MEDIATED IMMUNITY.

Gupta S
Clinical Immunology Service, Sloan-Kettering Inst., New York, NY
Clin Bull; 11(2):58-65 1981

The association between Hodgkin's disease and immunodeficiency states is reviewed. Immunodeficiencies may predispose patients with Hodgkin's disease to a second neoplasm and to increased risk of infectious complications, especially viral and fungal (eg herpes zoster and cryptococcosis). Both in vivo and in vitro T cell-mediated immune responses in patients with various stages of Hodgkin's disease are discussed, including delayed type hypersensitivity, homograft rejection, lymphocyte response to soluble antigens and to mitogens and allo-antigens, analysis of T cells and T cell subsets, and cytotoxic response and mechanisms responsible for T cell-mediated immunodeficiencies. The role played by splenectomy in treatment of Hodgkin's disease is discussed. (71 Refs)

HUMORAL IMMUNOSUPPRESSIVE AGENTS

49. SUPPRESSION OF IMMUNOLOGIC FUNCTION AND DEGENERATION OF LYMPHOID ORGANS IN CYCLOPHOSPHAMIDE-TREATED TURKEYS.

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Am J Vet Res; 42(12):2122-2128 1981

Neonatal administration of 8-20 mg of cyclophosphamide (CY) in turkey poults resulted in a marked alteration in the morphologic features of all major lymphoid organs. Cyclophosphamide induced severe deficiency in antibody response to multiple injections of Brucella abortus and sheep RBC and in vitro proliferative response of peripheral blood leukocytes to concanavalin A. The morphologic regeneration of thymus and of thymus-dependent areas was marked in all major lymphoid organs by posttreatment day 15. This regeneration preceded functional recovery of the mitogenic response of peripheral blood leukocytes. The regeneration of the bursa and bursa-dependent areas in other lymphoid organs was minimal through posttreatment day 27. Thus, CY may be used effectively in turkeys as an immunosuppressive reagent. (Author abstract) (13 Refs)

50. IMMUNOSUPPRESSIVE PROPERTIES AND CIRCULATING LIFE OF ACHROMOBACTER GLUTAMINASE-ASPARAGINASE COVALENTLY ATTACHED TO POLYETHYLENE GLYCOL IN MAN.

Abuchowski A, Davis FF, Davis S
(c/o Davis, S.) Oncology/Hematology, Veterans Admin. Medical Center, East Orange, NJ, 07019
Cancer Treat Rep; 65(11/12):1077-1081 1981

The immunosuppressive effects and circulating life of Achromobacter glutaminase-asparaginase (GA) covalently attached to polyethylene glycol (PEG) were examined in human subjects following a single iv dose of 1,000 IU/m2. Plasma half-life of PEG-GA was 72 hr. Skin test reactivity to recall antigens (mumps and tuberculin) was lost in all four patients tested. In vitro phytohemagglutinin-induced blastogenesis, 'natural killing,' and phytohemagglutinin-induced cell cytotoxicity was diminished as long as enzyme levels were detectable. In vivo and in vitro activities returned to normal following total plasma clearance of enzyme. (Author abstract) (12 Refs)

51. IMMUNOLOGY OF PYELONEPHRITIS IN THE PRIMATE MODEL. II. EFFECT OF IMMUNOSUPPRESSION.

Roberts JA, Domingue GJ, Martin LN, Kim JC, Rangan SR
Dept. Urology, Delta Primate Center, 3 Rivers Road, Covington, LA, 70433
Invest Urol; 19(3):148-153 1981

Nonobstructive pyelonephritis was produced in the rhesus monkey (Macaca mulatta) by means of retrograde inoculation of Escherichia coli to the point of pyelotubular backflow. The effects of treatment with cyclophosphamide or azathioprine were determined. Commensal renal viruses were not activated by the immunosuppression, and thus did not complicate our results. Both cyclophosphamide and azathioprine prolonged the bacteriuria and produced more severe pathology. Cyclophosphamide decreased the leukocytic response and partially suppressed the antibody response. The increased amount of acute pyelonephritic lesions after treatment with this drug suggest that the antibody and inflammatory responses may be important protective mechanisms, particularly regarding prevention of abscesses. In contrast, azathioprine did not decrease the leukocytosis nor the antibody responses, but resulted in decreased in vitro responsiveness of lymphocytes to mitogens. The increased severity of chronic pyelonephritic lesions after azathioprine treatment suggests that the cellular immune response also may be an important protective mechanism during the late stages of the disease. The results thus indicate that the immune response is protective and is not directly responsible for the chronic scarring of pyelonephritis. (Author abstract) (28 Refs)

52. PURIFICATION AND CHARACTERIZATION OF AN IMMUNOSUPPRESSIVE FACTOR FROM OVARIAN CANCER ASCITES FLUID.

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Eur J Immunol; 11(10):780-788 1981

A nonspecific immunosuppressive factor present in malignant (ovarian carcinoma) ascites fluid has been purified by acid extraction from a high mol wt (greater than 200,000) complex followed by preparative isoelectric focusing on Bio-lyte media. It is an acidic protein (pI = 3.6) of mol wt 50,000 to 52,000 as estimated by gel filtration and composed of subunits of 25,000 to 26,000 estimated by sodium dodecyl sulfate polyacrylamide gel electrophoresis, under reducing conditions. It inhibits the phytohemagglutinin-dependent mitogenic response of normal peripheral blood lymphocytes by 50% at 2 ug/ml concentrations in vitro and suppresses 80% of the plaque-forming cell response to sheep RBC at 100 ug per mouse in vivo. Its chemical identity with any of the known plasma proteins has not been established. Its failure to stain with periodic acid Schiff's reagent indicates its minimal content of carbohydrates. It is susceptible to tryptic and pronase digestion but insensitive to deoxyribonuclease and ribonuclease digestion. A smaller suppressive factor identified in the same fluid appears to be a lymphotoxin; it differs from the acid-extracted nonspecific suppressive factor in its lack of susceptibility to trypsin. (Author abstract) (31 Refs)

53. IMMUNOSUPPRESSIVE PROPERTIES OF CERTAIN ANTITUMOR AGENTS.

Zhukova IB, Tolvinskaia LS, Divnogorskaia NN

Dept. Pharmacology, N. I. Pirogov Second Medical Inst., Moscow, USSR

Farmakol Toksikol; 44(5):625-630 1981

The immunosuppressive properties of the alkylating agents paphencyl, prospidin, promycil, and imidasole-4-carboxamide were studied in CBA mice. The cytostatics were administered ip 24 hr prior to, simultaneously with, and 24, 48, and 72 hr after immunization of the mice with sheep RBC. The first three cytostatics caused a dose-dependent decrease in the number of IgM-producing cell s. The most pronounced inhibition of antibody-formation was observed after the administration of the paphencyl. (24 Refs) (In RUS)

54. THE EFFECT OF CHRONIC DAILY CYCLOPHOSPHAMIDE ADMINISTRATION ON ESTABLISHED ANTIBODY RESPONSES.

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Clin Exp Immunol; 46(1):178-184 1981

Experiments are described in which the effect of prolonged daily cyclophosphamide administration on established antibody responses is assessed. The antigen used in this study was chicken RBC (CRBC) and IgG anti-CRBC antibody production was measured in an antibody-dependent cell-mediated cytotoxicity assay. It is concluded that prolonged administration of cyclophosphamide does cause a small fall in the level of IgG antibody production. This fall, however, is rapidly reversed when the drug is withdrawn. These data suggest that any clinical benefit of cyclophosphamide in the treatment of diseases with autoimmune phenomena may not be due to the action of the drug on antibody-producing cells or their precursors. (Author abstract) (45 Refs)

OTHER RELATED STUDIES

55. IMPAIRED B-LYMPHOCYTE REACTIVITY IN PATIENTS WITH HODGKIN'S DISEASE AND NON-HODGKIN-LYMPHOMAS.

Ruhl H, Enders B, Bur M, Sieber G

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Blut; 42(5):271-281 1981

The ability of B cells to differentiate into immunoglobulin-secreting cells (ISC) was studied by a reverse hemolytic plaque assay in 42 patients with Hodgkin's disease (HD) and 33 patients with non-Hodgkin lymphomas (NHL). Forty healthy individuals served as controls. Induction of ISC was triggered by pokeweed mitogen, with optimum response in all groups at concentrations of 1.0-15.0 al/ml. Mean numbers of ISC (x 10(-2)/10(6) peripheral blood lymphocytes) were 4,370 for HD patients and 2,450 for NHL patients. Mean control value was 10,540. Most HD and NHL patients showed reduced response. No clear correlation between response and patient age could be demonstrated. Response in HD patients decreased with progression of disease, although most patients in remission were still below normal. Coculturing of HD or NHL lymphocytes with normal lymphocytes indicated the NHL response deficiency was due to a B cell defect, T cell function being normal. HD deficiency was due to a B cell defect plus defects in T helper cells and suppressor cells. HD deficiency is evidently reversible and can be corrected with appropriate therapy. (38 Refs)

56. VARIATION OF INTERFERON INDUCTION AT THE BONE MARROW LEVEL. STUDIES ON INTERFERON INDUCTION IN RELATION TO NATURAL CELL-MEDIATED CYTOTOXIC MECHANISMS.

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Ear J Immunol; 11(10):795-799 1981

The effects of interferon inducers on different cytolytic mechanisms were studied in the high leukemia mouse strain

AKR. A clear depression in baseline cytolytic potential and interferon-mediated stimulation of natural killer cell activities was demonstrated. This depression was most pronounced after 8 wk of age. In contrast, antibody-dependent, cell-mediated cytotoxicity against IgG-coated chicken RBC was always normal. Bone marrow chimeras between CBA and AKR mice were produced to investigate the influence of bone marrow vs host-mediated factors in these two strains with regard to interferon induction and cytolytic functions. Bone marrow genotype was found to be the dominating factor with regard to both parameters. Mice reconstituted with AKR bone marrow were deficient both in interferon production using tilorone and Newcastle disease virus as inducers, and at the level of natural killer cells responding to exogenously administered interferon. The possible relationship between these findings and the development of lymphomas in AKR mice is discussed. (Author abstract) (32 Refs)

57. ASSOCIATION OF MICROTUBULES AND INTERMEDIATE FILAMENTS IN NORMAL FIBROBLASTS AND ITS DISRUPTION UPON TRANSFORMATION BY A TEMPERATURE-SENSITIVE MUTANT OF ROUS SARCOMA VIRUS.

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Proc Natl Acad Sci USA; 78(11,part2):6986-6990 1981

By double indirect immunofluorescence, using primary rabbit antibodies to tubulin and guinea pig antibodies to vimentin, we have simultaneously labeled microtubules and intermediate filaments in several types of cultured normal fibroblasts. With well-spread interphase cells there was an extensive but not complete correspondence of the labeling patterns for the two filamentous structures out to the cell periphery. This correspondence existed both at a gross level, where parallel but not coincident arrays of thickly labeled strands of the two types of filaments were observed, and at a fine level, where thinly labeled strands of the two were superimposed. The results suggest that there may be some type(s) of molecular linkages between microtubules and vimentin intermediate filaments that is under metabolic control. With NRK fibroblasts infected with a temperature-sensitive mutant (LA23) of Rous sarcoma virus, cells grown at the nonpermissive temperature (39 C) showed the correspondence of the distributions of the microtubules and intermediate filaments characteristic of the normal phenotype but within 1 hr after a shift to the permissive temperature (33 C) there was an extensive retraction of the intermediate filaments around the cell nucleus whereas the microtubules remained dispersed into the cell periphery. These results suggest t hat one of the functions carried out by p60src, the protein kinase responsible for transformation by Rous sarcoma virus, may be to modify the component(s) involved in the putative linkages between microtubules and intermediate filaments in the normal cells. (Author abstract) (26 Refs)

58. CHARACTERIZATION OF THE PHYTOHEMAGGLUTININ-INDUCED PROLIFERATING LYMPHOCYTE SUBPOPULATIONS IN CHRONIC LYMPHOCYTIC LEUKEMIA PATIENTS USING A CLONOGENIC AGAR TECHNIQUE AND MONOCLONAL ANTIBODIES.

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Blood; 58(5):1053-1055 1981

Peripheral blood lymphocytes from normal donors and patients with chronic lymphocytic leukemia, B-cell type, were purified into T, helper T, and suppressor T lymphocytes by fluorescence-activated cell sorting using OKT3, OKT4, and OKT8 monoclonal antibodies. The max response of the purified subpopulations to stimulation by phytohemagglutinin (PHA) was determined by measuring the production of colonies when the stimulated cells were grown on agar. The helper T cells in normal and CLL patients were the most responsive to PHA stimulation, although the responsiveness of helper T cells to PHA was decreased in CLL. Purified CLL B cells responded minimally to PHA stimulation, but normal B lymphocytes did not. The abnormal response of CLL lymphocytes to PHA appears to be due to abnormal helper T cells, and, to a smaller extent, to the ability of CLL B lymphocytes to respond. (Author abstract) (17 Refs)

59. ANATOMIC PATHOLOGY: A NEW ENZYME IMMUNOLECTIN TISSUE STAIN.

Robb JA

Dept. Pathology, Green Hosp. Scripps Clinic, La Jolla, CA

Diagn Med; 4(7):87-89,92-95 1981

An enzyme-linked immunolectin histochemical staining technique for identification of disease processes in tissue samples is described. The method uses a glucose oxidase-avidin-biotin (GAB) antibody complex to amplify primary antigen-antibody interactions. GAB assay has high sensitivity and is free of background interference. Antigens can be detected in any location or amount. The assay is easily reproduced and does not require extensive training of pathologists. Applications include the detection of normal cellular products (including keratin, anterior pituitary hormones, and ABO blood group antigens), infectious agents, and lymphocyte surface markers. GAB assay makes it possible to differentiate between various types of herpetoviruses and may eventually be useful for detection of tumor-specific antigens. The method can detect many, if not all, antigens in formalin-fixed tissue specimens. (11 Refs)

60. PHILADELPHIA CHROMOSOME POSITIVE BLOOD B LYMPHOCYTES IN CHRONIC MYELOCYTIC LEUKEMIA.

Bernheim A, Berger R, Preud'homme JL, Labaume S, Bussel A, Barot-Ciorbaru R

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Leuk Res; 5(4/5):331-339 1981

An assay was developed to determine by combined study, using surface immunofluorescence and Q banding, the presence of surface immunoglobulins (SIg) on Philadelphia chromosome (PH1)+ mitotic cells obtained by stimulation of blood mononuclear cells by B cell mitogens. Cells were obtained from 18 patients (11 men, 7 women, 26-76 yr old) with typical PH1+ chronic myelocytic leukemia. Clear-cut results were obtained in eight cases. The incidence of Ph1+ and Ph1-mitoses was similar in the combined assay and in the regular cytogenetic study. No problems were encountered with SIg staining; the numbers of SIgM-bearing cells were the same in the combined assay in the controls with direct surface staining alone. In the combined assay, Ph1+ SIgM+ cells were found in all patients but only in stimulated cultures. Their presence was associated with B cell stimulation. With the exception of one culture, all SIgM-bearing cells with identifiable chromosome morphology had the Ph1 marker. In unstimulated cultures, every mitosis contained the Ph1 as shown by both single and combined chromosomal analyses. The combined study showed that these spontaneously dividing leukemic cells lacked SIgM. In contrast to control experiments, cultures stimulated with pokeweed mitogen or L881 fraction from Nocardia opaca contained a large number of Ph1-SigM- mitotic cells which were probably stimulated T-cells. (17 Refs)

61. LOCALIZATION OF PHOSPHOPROTEIN C23 TO NUCLEOLAR STRUCTURES AND TO THE NUCLEOLUS ORGANIZER REGIONS.

Lischwe MA, Richards RL, Busch RK, Busch H

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Exp Cell Res; 136(1):101-109 1981

After extraction of Novikoff hepatoma nucleoli with 4 M urea/3 M LiCl, phosphoprotein C23 was isolated by DEAE-cellulose and Bio-Rad AG3-X4A column chromatography. Immunization of rabbits with the highly purified protein C23 resulted in the production of a specific antibody as determined by Ouchterlony diffusion analysis. When the immunoperoxidase method was used to localize protein C23 in cells, it was found in 'fibrillar centers' (nucleolonemas) in nucleoli. Protein C23 was also demonstrated to be present on the nucleolus organizer regions (NORs) of metaphase chromosomes. (Author abstract) (33 Refs)

62. EVIDENCE FOR TWO DISTINCT POPULATIONS OF SUPPRESSOR CELLS IN THE SPLEENS OF MYCOBACTERIUM BOVIS BCG-SENSITIZED MICE.

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Infect Immun; 34(2):315-322 1981

Spleen cells from female C57BL/6 mice infected iv with 1 mg (about 10(7) viable units) of BCG were shown to suppress the blastogenic responses induced by the T-cell mitogens phytohemagglut inin and concanavalin A and by the B-cell mitogen lipopolysaccharide in spleen cells from normal syngeneic mice. By using various separation procedures or cellular treatments, evidence was found for two distinct populations of splenic suppressor cells. One population belonged to the monocyte-macrophage lineage on the basis of their adherence to plastic surfaces, their removal after treatment with carbonyl iron, and their resistance to gamma irradiation. The other population of suppressor cells belonged to the T lymphocytes due to their sensitivity to an anti-Thy 1 antiserum and complement and to gamma irradiation. After separation on nylon wool columns, inhibitory activity was found in both the nonadherent and the adherent spleen cell populations. Both populations of suppressor cells were present in the spleens 14 days after BCG inoculation and persisted for at least 40 days after infection. (Author abstract) (20 Refs)

63. IMMUNOREGULATION OF HUMAN MYELOPOIESIS.

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Dept. Developmental Therapeutics, Univ Texas M. D. Anderson Hosp. and Tumor Inst., Houston, TX

Cancer Bull; 33(5):218-220 1981

In the light of a proposed hypothesis, the attempt was made to investigate whether the cellular mechanisms that existed for the control of elaboration of colony-stimulating activity (CSA) - molecules essential for proliferation and differentiation of granulocyte-macrophage progenitor cells (GM-CFC) - were the same as those for production of immunoglobulins. Subjects discussed include: monocyte-macrophage and T-lymphocyte interaction for CSA elaboration; mechanisms of monocyte-macrophage and T-lymphocyte interactions for CSA elaboration; clinical application of the experimental data; and monocyte-macrophage inhibition of GM-CFC proliferation by direct cell contact. One of the important findings is that lithium carbonate blocked suppressor T-lymphocyte (TL) activation that would otherwise suppress CSA elaboration. Lithium carbonate was found to be beneficial in ameliorating the neutropenia in a case of preleukemic syndrome, oligoleukemic syndrome, and cyclic neutropenia. It is not beneficial in all types of neutropenic syndromes. The findings suggest lithium carbonate would work successfully only in those patients whose suppressor TL are the etiologic factor for their neutropenia. (12 Refs)

64. CONVERSION OF HERPETIC LESIONS TO MALIGNANCY BY ULTRAVIOLET EXPOSURE AND PROMOTER APPLICATION.

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J Gen Virol; 55(part2):305-313 1981

Many lines of evidence exist associating herpes simplex virus (HSV) with the development of carcinoma, but much of this evidence is anecdotal or associative in nature and does not prove a cause and effect. The purpose of this research was to investigate the oncogenic potential of HSV Type 2 (HSV-2) in vivo. A mouse model for lip carcinogenesis was designed to combine HSV-2 infection, UV exposure and tetradecanoylphorbol-acetate (TPA) application. HSV-2 inoculation on to abraded mouse lips was capable of causing vesicular ulcerative lesions which healed completely after 10 to 14 days. UV irradiation of the HSV lesion site daily for 6 min at 42 ergs/mm2/s on days 3 to 6 post-infection caused hyperkeratosis, acanthosis and dysplasia to develop in several lips; while the same UV exposure by itself failed to alter the histologic appearance. The addition of repeated TPA application to the HSV + UV regimen promoted tumor emergence. Thirty-two of 156 Balb/c mice developed tumors. Although the majority were papillomas, six were squamous cell carcinomas. These tumor-bearing mice had increased HSV-specific antibody titers. HSV antigens were shown to be present in outgrowths from explanted tumors as well as in tumor biopsies by immunoperoxidase staining with HSV-specific antisera. It is suggested that the in vivo UV-irradiated HSV acted as an inducer and TPA as the promoter, analogous to the classical two-stage carcinogenesis model. (Author abstract) (29 Refs)

65. PURIFICATION OF SPECIFIC ANTIBODY TO ALPHA-FOETOPROTEIN AND ITS IMMUNOLOGICAL EFFECT ON CANCER CELLS.

Hirai H, Tsukada Y, Hara A, Hibi N, Nishi S, Wepsic HT, Koji T, Ishii N
Dept. Biochemistry, Hokkaido Univ. Sch. Med., Sapporo, Japan
J Chromatogr; 215:195-210 1981

Human or rat alpha-fetoprotein (AFP) was highly purified from ascitic fluid or serum of hepatoma bearers. The purification was carried out mainly by means of immunoadsorbent chromatography using Sepharose coupled to specific anti-AFP antibody with BrCN activation, and by Sephadex gel filtration. Horses were immunized with the purified AFP and the specific antibody was isolated from the antiserum by means of an immunoadsorbent coupled to purified AFP. The specific antibody was found to bind specifically with AFP-producing tumor cells. The antibody was applied for radio immunodetection of the tumor. 125I-labeled antibody was administered to patients or rats with hepatoma, and radioactivity localized in the tumors was scintiscanned with a scintillation camera. In this way, the location of the tumor was detected in about 50% of the hepatoma bearers. The cytotoxicity of the antibody was clearly demonstrated both in vitro and in vivo in animal experiments. The antibody was administered to patients with advanced hepatoma. Although no improvement of the disease was demonstrated, serum AFP levels decreased greatly and in some cases low AFP levels were maintained for long periods suggesting that the antibody suppressed AFP-producing hepatoma cells. No significant side effects were observed in patients who had been administered with the horse antib ody. (Author abstract) (10 Refs)

66. PROLONGED INCUBATION TIME IN IMMUNOHISTOCHEMISTRY: EFFECTS ON FLUORESCENCE STAINING OF IMMUNOGLOBULINS AND EPITHELIAL COMPONENTS IN ETHANOL- AND FORMALDEHYDE-FIXED PARAFFIN-EMBEDDED TISSUES.

Brandtzaeg P
Histochemical Lab., Inst. Pathology, Natl. Hosp., Rikshospitalet, Oslo, Norway
J Histochem Cytochem; 29(11):1302-1315 1981

By prolonging the incubation time from 30 min to 20 hr at room temperature, fluorochrome conjugates may be applied at about 10 x higher dilution and yet produce specific immunofluorescence staining of enhanced intensity. This modification of the direct method is important for reagent economy and, in addition, affords improved staining features for all antigens tested in formaldehyde-fixed tissues. It is particularly valuable when paired staining is used to characterize lymphoproliferative B-cell processes in pathological routine material; a clear-cut distinction between polyclonal and monoclonal expression of cytoplasmic Ig is obtained, and cells giving rise to a false staining pattern are easily pinpointed. It is likewise advantageous to use prolonged incubation with conjugate for the localization of Ig-producing and Ig-bearing B cells in saline-extracted ethanol-fixed tissues, and the same holds true for Ig and C3 in immune-complex deposits. Also IgE on the surface of mast cells in tissues from atopic subjects is visualized distinctly with this modification. However, the localization of epithelial components is not consistently improved in ethanol-fixed tissues when the incubation time is prolonged; secretory products such as lactoferrin, lysozyme, amylase, and secretory component (SC) are not always immobilized sufficiently by ethanol fixation to avoid diffusion artifacts and a substantial loss from the cytoplasm. Differences in intracellular storage probably contribute to the variable antigen stability. (Author abstract) (56 Refs)

67. NATURAL ANTIBODIES CARRYING A CROSS-REACTIVE IDIOTYPE ENHANCE TUMOR GROWTH IN THE RAT.

Natori T, Takahashi S, Nakagawa H, Aizawa M, Itaya T
Dept. Pathology, Hokkaido Univ. Sch. Medicine, Sapporo 060, Japan
Int J Cancer; 28(5):591-599 1981

A population of Fab fragments was identified in the papain-solubilized fraction of membranes of a rat chemically-induced sarcoma, KMT 17. The Fab fragments were partially purified by gel filtration and column electrophoresis. A rabbit antiserum against the partially purified Fab fragments was raised and shown to be specific for Fab fragments by immunoelectrophoresis. Furthermore, four lines of evidence indicated that the KMT 17 Fab fragments carry a cross-reactive idiotype: (1) the antiserum could bind only with a restricted population of normal Fab fragments having a pI of 6.3; (2) an unrelated antibody (WKA anti-SRBC) showed a weak cross-reactivity (less than 6%); (3) syngeneic antisera against the KMT 17 could bind with the 125I-KMT 17 Fab preparation that was purified by an immunoabsorbent column with the rabbit anti-KMT 17 Fab antiserum (anti-idiotype antibody); (4) the rabbit anti-KMT 17 Fab antiserum could bind with neither heavy nor light chains of WKA IgG. The natural antibody carrying the idiotype was found in normal serum and in various organs as well, especially in the lung of the conventional rats. In addition, the fractions containing Fab fragments (FrII) were shown to enhance tumor growth when injected into syngeneic animals, whereas Fab-free fractions that were separated from the Fab fragments by column electrophoresis showed no enhancing activity. These results strongly suggested that a population of Fab fragments carrying a cross-reactive idiotype was responsible for the enhancement of tumor growth. Mechanisms for the biological function of natural anti-tumor antibodies carrying a cross-reactive idiotype are discussed. (Author abstract) (31 Refs)

68. GENETIC AND CLINICAL STUDIES OF SERUM BETA2-MICROGLOBULIN LEVELS IN HAEMATOLOGICAL MALIGNANCIES.

Nakao Y, Matsumoto H, Miyazaki T, Watanabe S, Masaoka T, Takatsuki K, Kishihara M, Kobayashi N, Hattori M, Fujita T
Third Div., Dept. Medicine, Kobe Univ. Sch. Medicine, Chuoku, Kobe 650, Japan
Clin Exp Immunol; 46(1):134-141 1981

Sera from 244 patients with hematological malignancies were examined for beta2-microglobulin (beta2m) levels. There were 142 leukemias, 32 malignant lymphomas, 3 immunoblastic lymphomas, 2 pseudolymphomas and 65 multiple myelomas. Culture supernatants from various established cell lines were also tested. The phenotype facilitating beta2m shedding from the cell surface appeared to be independent of the specific IgG heavy chain allotypes; however, a myeloma group with normal serum beta2m levels showed a significant association with the specific Gm allotypes. The determination of serum beta2m levels can provide valuable information on the proliferative stage of the disorders, the effectiveness of chemotherapy, and be a diagnostic aid for blastic crisis in chronic myelocytic leukemias, and for subtyping lymphoid malignancies. (Author abstract) (30 Refs)

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Antibodies and Humoral Immunity

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TUMOR ANTIBODY PRODUCTION/ CHARACTERIZATION/ DETECTION

1. DEMONSTRATION OF AN ANTIBODY AGAINST PLATELET-DERIVED GROWTH FACTOR.

Heldin CH, Westermark B, Wasteson A
Inst. Medical and Physiological Chemistry, Uppsala Univ., S-751 23 Uppsala, Sweden
Exp Cell Res; 136(2):255-261 1981

An antibody was raised in a rabbit against platelet-derived growth factor (PDGF), purified from human platelets. It recognized specifically 125I-labeled PDGF, as demonstrated by

HE 20. 3173/2:

gel electrophoretic analysis of precipitated radioactivity. Addition of immunoglobulins from the immune serum to cell cultures together with PDGF inhibited the multiplication-stimulating activity of the growth factor. Further, multiplication-stimulating activity in crude platelet lysate was retained upon passage over a column of Sepharose-bound anti-PDGF; it was recovered after elution of the column with acid. A radioimmunoassay for PDGF was developed, permitting the determination of 5 ng PDGF/ml. Platelet factor 4 and beta-thromboglobulin, both being proteins of the platelet alpha-granule, did not cross-react in the radioimmunoassay for PDGF. The radioimmunoassay was utilized to examine the immunological relationship between PDGF and some other growth factors. The anionic growth factors previously demonstrated in platelets were found to be antigenically distinct from cationic PDGF. Similar results were obtained with epidermal growth factor (EGF) or fibroblast growth factor (FGF). In contrast, osteosarcoma-derived growth factor, a PDGF-like growth factor previously known as a product of cultured human osteosarcoma cells, showed some cross-reactivity in the radioimmunoassay for PDGF. It was concluded that osteosarcoma-derived growth factor (ODGF) has both physical-chemical and immunological properties in common with PDGF. (Author abstract) (20 Refs)

2. AN ENZYME LINKED IMMUNOSORBENT ASSAY FOR LEUCOCYTE AND PLATELET ANTIBODIES.

Doughty R, James V, Magee J
Regional Transfusion Center, Longley Lane, Sheffield S5 7JN, England
J Immunol Methods; 47(2):161-169 1981

An enzyme linked immunosorbent assay (ELISA) method for the detection of antibodies to platelets and leukocytes is presented. The method can be used for large numbers of samples. The method is objective when photometers are used. Approximately 50% of all cases of possible autoimmune thrombocytopenic purpura and unexplained neutropenia showed positive results. The results obtained using ELISA and standard tests for leukocyte and platelet antibodies are compared. The ELISA tests may also detect immune complexes. (Author abstract) (19 Refs)

3. A MONOCLONAL ANTIBODY WHICH IDENTIFIES A SUBPOPULATION OF HUMAN B LYMPHOCYTES AND MONOCYTES (MEETING ABSTRACT).

Munchus MS, Levitt D
University of Illinois Medical Center, Chicago, IL, 60612
Hybridomas and Cellular Immortality (Second Houston Symposium), November 5-6, 1981, Houston, Texas. University of Texas Medical School at Houston 55 pp., 1981.

Hybridoma antibodies were produced against the 'pre-B' lymphoblastoid cell line, Nalm-6. A subclone of one of these hybridoma antibodies (1-96) identifies a determinant on the surface and in the cytoplasm of Nalm-6 and 6 of 11 human lymphoblastoid cell lines. The intensity of reaction of 1-96 was greatest in cell lines with large numbers of cytoplasmic vesicles. I-96 identifies a different determinant than another monoclonal antibody specific for a common acute lymphoblastic leukemia antigen (J5). Furthermore, MABI-96 specifically reacts with a surface determinant on a subpopulation of slg+ and clg+ cells from peripheral blood, spleen, and tonsil, and with a subpopulation of G-10 adherent, OKMI+ cells. The I-96 antigen does not associate preferentially with any class of immunoglobulin and I-96 does not react with T cells. When PBMC are stimulated with the polyclonal B cell activators pokeweed mitogen and Staphylcoccus aureus (Cowans I) the number of MABI-96+/slg+ cells decreases sharply. In unstimulated cultures the percentage of such cells markedly increases by day 4, followed by a gradual decrease toward the end of the culture period. It appears that this antibody defines a functional subpopulation of human B lymphocytes and monocytes. (no Refs)

4. ECTOPIC ACTH PRODUCTION WITH AUTOANTIBODY FORMATION IN A PATIENT WITH ACUTE MYELOBLASTIC LEUKEMIA.

Pfluger KH, Gramse M, Gropp C, Havemann K
Abt. Hamatologie/Onkologie, Zentrum fur Innere Medizin, 3550 Marburg/Lahn, W. Germany
N Engl J Med; 305(27):1632-1636 1981

The case history of an acute myeloblastic leukemia (AML) patient with abnormal ACTH production and autoantibody formation is presented. Symptoms included anemia and slowly healing skin lesions. Differential blood profile revealed 60% lymphocytes, 30% blasts, and 10% granulocytes. Blood chemistry was abnormal; ACTH levels were 1960 picog/ml. Bone marrow was characteristic of AML. Therapy included doxorubicin, vincristine, and cytarabine. Remission followed, ACTH levels decreased but never reached normal levels. A subsequent marked rise in ACTH was unaccompanied by indications of relapse. A relapse did occur eventually; during relapse ACTH levels were about the same as during remission. Gradually the disease became progressive. No adenoma of pituitary or adrenal glands was revealed after death. The frequency of elevated ACTH in acute leukemia patients was also investigated by radioimmunoassay of serum, ultracentrifugation, polyacrylamide gel electrophoresis, and cell culture. Results showed only marginally elevated ACTH levels in most patients with various types of hemoblastosis. Apparently ectopic ACTH is produced in the leukemia cells. (31 Refs)

5. OSTEOSARCOMA PATIENTS: ISOLATION OF SERUM ANTIBODIES BY AFFINITY CHROMATOGRAPHY.

Tsang KY, Fudenberg HH, Gnagy MJ
Dept. Basic and Clinical Immunology and Microbiology, Medical Univ. South Carolina, Charleston, SC, 29403
JNCI; 67(6):1183-1189 1981

Antibodies specific for membrane-associated antigens of human osteosarcoma cells were isolated from sera of 12 patients with (OS). Affinity columns were prepared by coupling partially purified membrane antigens from cultured human OS cell lines (TE-85 or LM) to CBrN-activated Sepharose 4B. The antigens were prepared by discontinuous sucrose gradient ultracentrifugation, papain digestion, and DEAE column chromatography. Diluted serum was passed over the affinity columns, and the adsorbed proteins were eluted with 2.5 M $MgCl_2$ (pH 6.5). Immunodiffusion, indirect immunofluorescence, and complement fixation were used to assay antibody activity in the eluate. Specific anti-OS activity was found in the immunoglobulin (Ig) fraction isolated from the sera of the 12 OS patients, as confirmed by blocking experiments. No anti-OS antibody activity was found in sera from healthy individuals or patients with breast carcinoma, clear cell carcinoma, liposarcoma, or leukemia in this study. The anti-OS activity of the isolated Ig from OS patients was abolished after absorption with cultured human OS cells from lines LM, TE-85, or G292 but not after absorption with cells from lines WI-38 (embryonic lung), TE-32 (rhabdomyosarcoma), CAMA-1 or SW527 (breast carcinoma), or M-14 (melanoma). Absorption with rabbit antihuman IgG but not with rabbit antihuman IgM immunobeads completely eliminated the antibody activity. (Author abstract) (36 Refs)

6. WANDERING AROUND THE CELL SURFACE-MONOCLONAL ANTIBODIES AGAINST HUMAN NEUROBLASTOMA AND LEUKEMIA CELL SURFACE ANTIGENS (MEETING ABSTRACT).

Feder M, Jonak Z, Smith A, Glick MC, Kennett RH
Department of Human Genetics, University of Pennsylvania School of Medicine, Philadelphia, PA, 19104
Hybridomas and Cellular Immortality (Second Houston Symposium), November 5-6, 1981, Houston, Texas. University of Texas Medical School at Houston 55 pp., 1981.

Monoclonal antibodies have been made against cell surface antigens on human neuroblastoma cell lines and leukemia cell lines. These antibodies were tested against a panel of human cell types to define those antibodies having a restricted specificity. We will describe the use of monoclonal antibodies for detection of metastasis of neuroblastoma cells to bone marrow. Using a combination of two monoclonal antibodies we are able to detect and identify neuroblastoma cells and to distinguish them from normal and malignant lymphoid cells. We have also used these antibodies to isolate the cell surface glycoproteins by affinity chromatography. The glycoprotein antigens isolated from different tumor cell lines have been isolated and compared. One of the most promising applications of anti-tumor monoclonal antibodies may be the detection of cell surface molecules involved in the processes of cell growth and cell division. We have identified three monoclonal antibodies which inhibit the growth of the leukemia cell line Reh. The detection of these antibodies and their use in characterization of cell surface receptors will be discussed. (no Refs)

7. ANTIGENS DISPLAYED ON MURINE B LYMPHOCYTE PRECURSORS.

Kincade PW, Lee G, Watanabe T, Sun L, Scheid MP
Sloan-Kettering Inst. Caner Res., 145 Boston Post Road, Rye, NY, 10580
J Immunol; 127(6):2262-2268 1981

The surface antigen phenotype of the immediate precursors of clonable B Lymphocytes was investigated with conventional alloantisera and monoclonal antibodies directed to B lineage antigens. Ia was demonstrable on B cells, but not their immediate precursors in adult marrow. Adult, but not fetal, B cell precursors were susceptible to lysis with anti-Lyb-2 or Anti-Qa. A panel of monoclonal rat antibodies was prepared and placed into categories on the basis of recognition patterns obtained with established cell lines. Of two groups that are described here, in one (typified by antibodies from clone 14.8) we detect an antigen that is preferentially expressed on B cells and their precursors, a proportion of antibody-secreting cells, and a subpopulation of peripheral T lymphocytes. Cells that did not display demonstrable amounts of antigen include brain, granulocytes, macrophages, mastocytoma cells, and erythroleukemia cells. A second category of antibodies revealed an antigen that was more widely distributed on hemopoietic cells. Cells capable of quickly maturing into functional, colony-forming B lymphocytes in culture or after transfer to irradiated recipients specifically adhered to 14.8 antibody-coated, polystyrene petri dishes in the cold. Reductions in numbers of stem cells (CFU-s) and myeloid progenitors (CFU-c) by this treatment were minimal. Of particular importance was the fact that these antibodies recognized cells in embryonic liver as well as in adults that were destined to become B lymphocytes. These observations provide new perspective on B lineage precursor heterogeneity and suggest ways of localizing and dissecting some of the earliest events that are critical to development of the humoral immune system. (Author abstract) (51 Refs)

8. MONOCLONAL ANTIBODIES TO ANTIGENS OF HUMAN MELANOMA (MEETING ABSTRACT).

Brown JP, Hellstrom I, Hellstrom KE
No affiliation given
Hybridomas and Cellular Immortality (Second Houston Symposium), November 5-6, 1981, Houston, Texas. University of Texas Medical School at Houston 55 pp., 1981.

Monoclonal antibodies were used to identify and characterize antigens of human melanoma. Spleen cells from mice immunized with melanoma cells were fused with mouse myeloma cells. The hybrids were screened both by binding assays and by immunoprecipitation. One of the most interesting antigens identified is p97, a 97,000 mol wt cell surface glycoprotein, which is present in most melanomas but in only trace amounts in normal adult tissue. However, certain fetal tissues contain significant amounts of p97. Monoclonal antibodies to a number of distinct antigenic determinants of p97 have been used to develop a 2-site immunoradiometric assay, to obtain syngergistic complement-dependent cytotoxicity, for preparation of immunotoxins and for imaging studies. P97 has been purified from detergent-lysates of cultured melanoma cells by affinity chromatography with monoclonal antibody and Staphylococcus aureus protein A coupled to Sepharose. Amino acid sequencing studies of the purified protein have revealed that the N-terminal amino acid sequences of p97 and transferrin are homologous. The structure homology of p97 and transferrin was confirmed serologically using a mouse antiserum to denatured p97. Like transferrin, p97 binds iron. We conclude that melanoma-associated antigen p97 is evolutionarily and functionally related to transferrin, although its exact role in melanoma cells remain to be elucidated. (no Refs)

9. A BIOCHEMICAL AND BIOSYNTHETIC ANALYSIS OF HUMAN-MELANOMA-ASSOCIATED ANTIGENS WITH MONOCLONAL ANTIBODIES (MEETING ABSTRACT).

Bumol TF, Harper JR, Chee DO, Reisfeld RA
Scripps Clinic and Research Foundation, La Jolla, CA, 92037
Hybridomas and Cellular Immortality (Second Houston Symposium), November 5-6, 1981, Houston, Texas. University of Texas Medical School at Houston 55 pp., 1981.

Two monoclonal antibodies (MoAbs 9.2.27 and F11) directed to cell surface and secreted melanoma associated antigens, respectively, were used to study the expression, biosynthesis and molecular nature of these glycoconjugated molecules. MoAb 9.2.27 detected from 1-2 x 10(5) antigenic sites per cell in direct binding studies of several melanoma cell lines. Analysis of subcellular fractions of these cells by the same method indicated that nearly all antigenic activity was in crude membrane fractions. Sodium dodecyl sulfate -polyacrylamide gel electrophoresis (SDS-PAGE) analyses of immunoprecipitates of detergent extracts from biosynthetically labelled M21 melanoma cells showed that MoAb 9.2.27 recognizes a 250 kilodalton (250K) molecule together with a high mol wt component (HMW-C), Mr greater than 500,000 dalton. Pulse-chase analysis of this antigen complex in extracts of 35S-methionine labelled cells, treated with either the monovalent ionophore monensin or endoglycosidase H, revealed that MoAb 9.2.27 recognizes the 250K N-linked glycoprotein in the absence of the HMW-C as well as several precursor glycoproteins ranging from 210-240K. The chondroitin sulfate nature of the HMW-C was indicated by its ability to label with 35S-sulfate ion and its sensitivity to beta elimination and proteoglycan-specific enzymes chondroitinase ABC and AC lyases. MoAb F11 recognizes a glycoprotein of 100 kilodalton (100K) that has limited cell surface expression as it is secreted into spent culture media of melanoma cells. Pulse-chase analysis revealed the 100K antigen to be secreted at a slower rate than other major melanoma-associated glycoproteins, ie, fibronectin, suggesting a unique biosynthetic pathway. The 100K antigen is heavily glycosylated as evidenced by sensitivity to neuraminidase and biosynthetic alterations induced by monensin. Two monoclonal antibodies could thus be used effectively for an in depth study of biosynthetic and biochemical aspects of glyco-conjugated tumor associated antigens, paving the way for an analysis of their biological function in metastatic melanoma. (no Refs)

10. GENERATION OF MONOCLONAL ANTIBODIES REACTING WITH HUMAN NORMAL AND NEOPLASTIC MAMMARY DUCT EPITHELIAL CELLS (MEETING ABSTRACT).

Menard S, Colnaghi MI, Tagliabue E, Canevari S, Fossati G, Sonnino S
Istituto Nazionale Tumori, Milano, Italy
Hybridomas and Cellular Immortality (Second Houston Symposium), November 5-6, 1981, Houston, Texas. University of Texas Medical School at Houston 55 pp., 1981.

A monoclonal antibody was obtained from a hybridoma line generated by the fusion of P3 myeloma cells with spleen cells of a mouse immunized with cell membrane extracts from the human breast cancer cell line MCF-7. The specificity was studied by isotopic immunoglobulin assay on several cell lines and cell membrane extracts from various surgical specimens and milk cells; by membrane immunofluorescence on cell lines and cell suspensions obtained from fresh tumors; by immunofluorescence and immunoperoxidase technique on histological slices from about 100 different normal or neoplastic tissues. The structure recognized by the monoclonal antibody was found on normal epithelial cells of mammary duct and on 80% of the 50 breast carcinomas tested. The antigenic activity was unaffected by treatment with trypsin, Vibrio cholerae neuraminidase and by heating the cells at 100C but was inactivated by treatment with methanol. When lipid extracts for MCF-7 membrane preparations were chromatographed on diethylaminoethyl cellulose Sephadex the antigenic activity was recovered only on the neutral ganglioside fraction. (no Refs)

11. MONOCLONAL ANTIBODIES TO HUMAN PROSTATE AND BLADDER TUMOR ASSOCIATED ANTIGENS (MEETING ABSTRACT).

Starling JJ, Wright GL
Eastern Virginia Medical School, Norfolk, VA, 23501
Hybridomas and Cellular Immortality (Second Houston Symposium), November 5-6, 1981, Houston, Texas. University of Texas Medical School at Houston 55 pp., 1981.

Monoclonal antibodies to human prostate adenocarcinoma membrane antigens were produced by fusion of spleen cells from Balb/C mice immunized against the prostate cancer cells line DU145, and the P3X63/Ag8 mouse myeloma line. The hybrids were screened for antibody production using glutaraldehyde-fixed or live cells in an in vitro binding radioimmunoassay (RIA). Antibody binding specificity was also checked by quantitative adsorption studies. A hybridoma clone (83.21) was isolated that secreted antibodies which preferentially bound to prostate and bladder cancer cells but did not bind to a variety of othe r normal and malignant human cell lines. This antibody also reacted with a cytomegalovirus-transformed human embryonic lung cell line but not to normal human embryonic lung cells. Conventional and competitive binding studies indicate that the 83.21 monoclonal antibody does not bind to alpha-fetoprotein, carcinoembryonic antigen, prostatic acid phosphatase, human WBC antigen (HLA), beta2 microglobulin, fibronectin, prostate specific antigen or DR antigens. Preliminary immunoprecipitation data with 125I-labeled, detergent soluble, DU145 membrane proteins and the 83.21 monoclonal antibody suggest that this antibody binds two proteins with mol wt of 210 and 97 kilodaltons. (no Refs)

12. APPLICATION OF MONOCLONAL ANTIBODIES TO THE STUDY OF HUMAN CANCER (MEETING ABSTRACT).

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Hybridomas and Cellular Immortality (Second Houston Symposium), November 5-6, 1981, Houston, Texas. University of Texas Medical School at Houston 55 pp., 1981.

Monoclonal antibodies are used by our group to define antigens of human solid tumors. Most of the antigens detected on the surface of human melanomas are glycoproteins. In the case of gastrointestinal (GI) tumors however, murine monoclonal antibodies are detected in the majority of cases against glycolipid moieties. Several of these antibodies stain strongly in immunoperoxidase procedure (Bouin's fixed, paraffin-embedded specimens). The distribution of a monosialoganglioside antigen in tissues was presently confirmed in immunoperoxidase assays. The antigen was present in 50% of colon carcinomas and in all carcinomas of pancreas (7/7) and stomach (4/4) tested. Breast (0/12) and lung (0/5) tumors were negative. Interestingly, antigen was also detected in 11/15 adenomatous polyps, including 6/8 villous adenomas. This antigen was also detected in pancreatic and hepatic ducts, bronchial glands and focally in gastric epithelium. The negative tissues included pancreatic acini, Langerhans islets, hepatocytes and epithelium of bronchial, colonic and gall bladder origin. Hybridomas established after immunization of tumor cells secreted antibodies directed against a variety of human blood group antigens. They include Leb antigen and two types of precursor substances common to the ABH and Lewis system: type 1 with beta 1, 3 linkage and type 2 with beta 1, 4 linkage of terminal galactose to N-acetylglucosamine. Four other monoclonal antibodies are specific for B group substances. Three are directed against type 2 chain and one against both chains. (no Refs)

13. MONOCLONAL ANTIBODIES SPECIFYING TUMOR ASSOCIATED ANTIGENS AND THEIR POTENTIAL FOR DIAGNOSIS AND THERAPY (MEETING ABSTRACT).

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Hybridomas and Cellular Immortality (Second Houston Symposium), November 5-6, 1981, Houston, Texas. University of Texas Medical School at Houston 55 pp., 1981.

Monoclonal antibodies specifying cell surface antigens on normal and malignant cells provide probes for investigating cell membrane changes in malignant transformation and for developing new approaches to cancer detection and treatment. Monoclonal antibodies directed against antigens associated with a naturally arising rat mammary carcinoma (Sp4) are produced by an interspecies hybridoma derived from a fusion of spleen cells from a syngeneic Sp4-immune rat with P3NS1 mouse myeloma cells. These antibody preparations (Sp4/A4) react specifically with tumor Sp4 cells when tested by membrane immunofluorescence or radioimmunoassays. The expression of Sp4 antigen on cells derived from tumors has also been demonstrated by analysis in the Fluorescence Activated Cell Sorter so providing a quantitative procedure for the analysis of cells derived from in vivo tumors. Sp4/A4 monoclonal antibody (rat IgG gamma 2b, mouse K chain) labelled with 125I specifically localizes in Sp4 tumor growing sc in syngeneic rats. Tumor localization was also demonstrated using 125I-labelled antibody by whole body gamma scintigraphy after 99mTc labelled blood pool subtraction. The therapeutic potential of conjugates of this antibody preparation conjugated to adriamycin have been evaluated. Adriamycin conjugated to antibody via a dextran bridge retained cytotoxic activity as assayed by an in vitro target cell survival. The conjugates also retained antibody activity binding to tumor Sp4 but not unrelated tumors. When tested in vivo the conjugates showed enhanced therapeutic effectiveness when tested against sc tumor grafts. (no Refs)

TUMOR ANTIBODIES ASSOCIATED WITH VIRUSES

14. CHLAMYDIA TRACHOMATIS AND HERPES SIMPLEX VIRUS IGA ANTIBODIES IN CERVICAL SECRETIONS OF PATIENTS WITH CERVICAL ATYPIA.

Kalimo K, Terho P, Honkonen E, Gronroos M, Halonen P
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Br J Obstet Gynaecol; 88(11):1130-1134 1981

The association of Chlamydia trachomatis (CT) and herpes simplex virus (HSV) with malignant or premalignant changes in the cervix uteri was studied by determining immunoglobulin A (IgA) antibodies in the cervical secretions of 28 women with inflammatory, 28 with dysplastic 7 with malignant changes of the uterine cervix, and 26 healthy controls. In cervical secretions IgA antibodies to CT were found in 24 of 35 (69%) patients with malignant or premalignant changes, in 11 of 28 (39%) with cervicitis and in 3 of 26 (12%) controls. IgA antibodies to HSV were found in 10 of 35 (28%) patients with malignant atypia or dysplasia but in none of the women with cervicitis or the controls. The highest frequency of antibodies was found in the patients with cervical carcinoma. Serum IgA antibodies to CT and HSV were found equally in the patients and the controls. Our results suggest that in patients with cervical atypia, local IgA CT antibody production occurs. Whether this association is etiological or coincidental cannot be concluded from this study. (Author abstract) (13 Refs)

15. THE IMMUNOREGULATORY CHARACTERISTICS OF THE LACTIC DEHYDROGENASE VIRUS (LDV), A COMMON CONTAMINANT OF TUMORS.

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Dept. Cell Biology, Weizmann Inst. Science, Rehovot, Israel
Cell Mol Biol; 27(2/3):83-96 1981

A tumor-enhancing and antibody increasing spleen cell-associated factor originating in Lewis lung carcinoma (3LL)-bearing C57BL/6 mice was identified as the lactic dehydrogenase virus (LDV). A potent immunoregulating factor was obtained only following the inoculation of LDV-infected but not LDV-free tumor cells. The observed augmentation of humoral responses by an acute infection with LDV was found to be fully correlated with the ability of the virus to replicate and establish a persisting infection in the host. LDV caused an augmented humoral response in all mouse strains tested (causing a life-long viremia), but failed to influence the humoral response in rats, which are an LDV-resistant species. We found that although an infection with LDV causes a polyclonal B-cell activation it does not affect all of the different B-cell clones and in the presence of a specific antigenic stimulus it preferentially triggers the IgG2 subclass of antibody-secreting B cells. An acute LDV infection causes a substantial suppression of cell-mediated immunity functions and a delayed thyroid allograft rejection was demonstrated in infected mice. Since mononuclear phagocytes, which are the target cells of LDV, play an important role in cellular immune responses, we tested the immunogenic antigen-presenting capacity of LDV-infected macrophages, using a system in which in vitro reactivation of memory T cells is dependent upon effective specific antigen presentation by macrophages. We found that the antigen presentation capacity of macrophages from acute LDV-infected mice is impaired. These results may contribute to a better understanding of the ways in which mammalian RNA viruses may act as immunomodulators. (Author abstract) (42 Refs)

16. INHIBITION OF T CELL-MEDIATED FUNCTIONS BY MVM(I), A PARVOVIRUS CLOSELY RELATED TO MINUTE VIRUS OF MICE.

Engers HD, Louis JA, Zubler RH, Hirt B
Dept. Immunology and Virology, Swiss Inst. Experimental Cancer Res., 1066 Epalinges, Switzerland
J Immunol; 127(6):2280-2285 1981

A purified preparation of MVM(i), a murine parvovirus closely related to minute virus of mice (MVM), was found to inhibit various functions mediated by murine T cells in vitro. Addition of MVM(i) virus to secondary allogeneic mixed leukocyte cultures resulted in the inhibition of both lymphocyte proliferation (3H-thymidine incorporation) and the generation of cytolytic T lymphocyte activity but not interferon production. MVM(i) virus also inhibited the growth and cytolytic activity of several cloned, long-term Lyt-2+ cytolytic T cell lines. Furthermore, the antigen-induced proliferative responses of parasite- (Leishmania) specific Lyt-1+ T cells in vitro was abrogated by the addition of MVM(i) virus to the culture. Finally, the suppression of an in vitro antibody response to SRBC by MVM(i) virus was the result of the inhibition of T helper cells required for the B cell response. These suppressive effects were specific for MVM(i); parallel studies in which the prototype MVM parvovirus was used showed no significant inhibition in the various systems tested. (Author abstract) (32 Refs)

17. AGE- AND SEX-RELATED DIFFERENCES IN ANTIBODY FORMATION AND BLASTOGENIC RESPONSIVENESS OF SPLENOCYTES FROM RIII MICE DEVELOPING VIRUS-INDUCED MAMMARY ADENOCARCINOMA.

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JNCI; 67(6):1347-1351 1981

Inbred RIII mice, known to be infected neonatally with murine mammary tumor virus so that females develop mammary adenocarcinoma by 12-15 mo. of age, were examined with regard to antisheep red blood cell antibody responses at the cellular level. Female mice, 3-11 mo old, compared to male mice of the same ages had consistent and significant depression of the antibody response of their splenocytes. Furthermore, female mice with adenocarcinoma showed an even greater depression of the antibody response. Spleen sizes were consistently increased in females as compared to those of male mice throughout the first yr of life. The blastogenic responsiveness of the splenocytes to the B-cell mitogen Escherichia coli lipopolysaccharide and the T-cell mitogen phytohemagglutinin-P was not significantly different between male and female mice during the same periods, although the responses of the older tumor-bearing female mice to phytohemagglutinin-P were lower than those of non-tumor-bearing female mice. A complex relationship between age, sex, and immune responsiveness was evident in these mammary tumor virus-infected mice, which made it difficult to attribute a specific immune event to emergence of the mammary adenocarcinomas in the female as compared to male mice. (Author abstract) (9 Refs)

ANTITUMOR ACTIVITY AND IMMUNOTHERAPY

18. SPECIFIC IMMUNOADSORPTION OF IGG ANTIBODY IN A PATIENT WITH CHRONIC LYMPHOCYTIC LEUKEMIA AND AUTOIMMUNE HEMOLYTIC ANEMIA: A NEW FORM OF THERAPY FOR THE ACUTE CRITICAL STAGE.

Besa EC, Ray PK, Swami VK, Idiculla A, Rhoads JE, Bassett JG, Joseph RR, Cooper DR
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Am J Med; 71(6):1035-1040 1981

Progressive and severe autoimmune hemolytic anemia developed in a patient with chronic lymphocytic leukemia (CLL) despite treatment with chlorambucil, high doses of corticosteroids and attempts to transfuse packed red blood cells. Splenectomy was not performed because of severe coronary artery disease. Direct antiglobulin tests revealed a warm red blood cell autoantibody of IgG-type with anti-e specificity. The patient was treated by extracorporeal immunoadsorption of plasma IgG using a cell separator and protein A as the immunoadsorbent. The patient responded by an increase in the hemoglobin levels and platelet counts after two treatments. Specificity of the procedure was shown by a decrease in the serum IgG and by the demonstration of the same reactivity to ficin-treated reagent red blood cell panel of the eluate from the protein A. Antibody titers of the patient's red blood cell eluate decreased from 1:128 to 1:64 and eventually the anti-e specificity was lost. This is a report of a novel approach to treatment of the acute phase of an autoimmune hemolytic anemia. (Author abstract) (22 Refs)

19. BONE MARROW TRANSPLANTATION IN ACUTE LEUKEMIAS: PROPHYLACTIC ANTIBODY TREATMENT FOR SUPPRESSION OF GRAFT-VERSUS-HOST DISEASE.

Rodt H, Netzel B, Kolb HJ, Haas RJ, Wilms K, Bender-Gotze C, Wernet P, Janka G, Link H, Wilmanns W, Thierfelder S, Munchner Arbeitsgemeinschaft fur KMT
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Blut; 43(2):113-118 1981

Suppression of graft-vs-host disease (GvHD) by antibody treatment was tested in patients with acute leukemias who had received bone marrow transplants. Anti-human T-cell-globulin (AHTZG) was prepared by adsorption of anti-human-thymocyte serum with liver/kidney homogenate, B cells from patients with chronic leukemia, and erythrocytes. The AHTZG was active against T-lymphocytes, but not against hemopoietic precursor cells in culture and diffusion-chamber assays. Patients were preconditioned by anti-leukemic chemotherapy and whole-body irradiation of 1,000 rads. Marrow transplants were obtained from compatible siblings. Ten patients were in relapse, and four were in remission at the time of transplant. Hemopoietic grafts were successful in 12 cases. No side effects were noted. Three patients showed cutaneous signs of GvHD, and two of them later developed GvHD in the liver. Five of 14 patients were alive and in remission 144-964 days after transplant. (14 Refs) (In GER)

20. MONOCLONAL ANTIBODIES REACTIVE WITH ACUTE MYELOGENOUS LEUKEMIA CELLS.

Linker-Israeli M, Billing RJ, Foon KA, Terasaki PI
1000 Veteran Ave., Room 15-22, Los Angeles, CA, 90024
J Immunol; 127(6):2473-2477 1981

Two cytotoxic monoclonal antibodies (D5D6 and C10H5) were raised to acute myelogenous leukemia (AML) cells. One of them, D5D6, reacted with 100% of the cells from 44/50 AML patients. The second, C10H5, reacted with 100% of the cells from 13/39 AML patients. D5D6 and C10H5 were cytotoxic to 100% of the monocytes from all healthy donors tested. Apart from monocytes, these antibodies did not react with any other peripheral blood cells from normal donors or with cancerous cells either from cell culture lines or from patients with chronic myelogenous leukemia (CML), lymphoid leukemias, or solid tumors. These antibodies inhibited the growth of the myeloid-monocytic stem cell, the CFU-C, and reacted with a minor population of normal bone marrow cells by immunofluorescence. Both D5D6 and CH5 have potential utility for the differential diagnosis of acute leukemia, for the detection of early leukemic relapse, and for enrichment of human stem cells. (Author abstract) (18 Refs)

21. IMMUNOPOTENTIATING ACTION OF STREPTOCOCCAL PREPARATION OK-432 AND PROTEIN-BOUND POLYSACCHARIDE PS-K ON DEPRESSED STATE OF CELL-MEDIATED AND HUMORAL IMMUNITIES OF FRIEND LEUKEMIA VIRUS INFECTED MICE.

Kiyohashi A
Dept. Internal Medicine, Sch. Medicine, Kitasato Univ., Japan
Nippon Gan Chiryo Gakkai Shi; 16(4):641-646 1981

The effects of OK-432, a penicillin-treated Group A hemolytic streptococci, and PS-K, a protein-bound polysaccharide, on the immune response of male ICR and ddY mice infected with Friend leukemia virus (FLV) were examined. FLV-infected mice were injected iv with either 0.5 KE (1 KE = 0.1 mg lyophilized streptococci) OK-432 or 30 mg/kg PS-K daily for 3 consecutive days, from 5 days before and from 3 days after FLV inoculation. Lymph node cells of mice treated with both FLV and OK-432 responded well to ovalbumin (OA) and purified protein tuberculin derivative in macrophage migration inhibition tests conducted 21-31 days after immunization with OA. Mice treated wtih FLV and PS-K showed no response. Both response of hemolytic plaque forming cells to sheep RBC (anti-SRBC PFC) and serum antibody production were not detected in the FLV-infected mice, whether injected with OK-432 or PS-K. The anti-SRBC PFC response and antibody production in OK-432-treated mice were slightly greater than those in the other FLV-infected groups, but the differences were not significant. The results suggested that OK-432 has an immunopotentiating activity on the depressed state of cell-mediated immunity, while PS-K does not. Neither PS-K nor OK-432 enhanced humoral immunity in FLV-infected mice. (13 Refs)

22. INHIBITION OF CUTANEOUS ANAPHYLAXIS AND ARTHUS REACTIONS IN THE MOUSE BY ANTIGEN-SPECIFIC IGA.

Russell-Jones GJ, Ey PL, Reynolds BL
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Int Arch Allergy Appl Immunol; 66(3):316-325 1981

The nitrophenyl-specific IgA myeloma protein secreted by the MOPC-315 mouse plasmacytoma was examined for its capacity to inhibit antibody-mediated hypersensitivity reactions in the mouse. Specific inhibition of both cutaneous anaphylactic and complement-dependent (Arthus) reactions was observed in sensitized mice when the eliciting antigen was mixed with IgA prior to injection or when the mice were injected with plasmacytoma cells and possessed detectable amounts of MOPC-315 IgA in their serum at the time of challenge. The possibility that IgA antibodies have a role in suppressing hypersensitivity reactions at mucosal surfaces is discussed. (Author abstract) (31 Refs)

23. MONOCLONAL ANTIBODIES SPECIFYING TUMOUR-ASSOCIATED ANTIGENS AND THEIR POTENTIAL FOR THERAPY.

Baldwin RW, Embleton MJ, Price MR
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Mol Aspect Med; 4(5):329-368 1981

Technique for the production of monoclonal antibodies (MA) is described. A review of MA studies in animals is followed by personal experiences with the use of MA in human osteogenic sarcoma and malignant melanoma. Use of MA in other human tumors, as described in the literature, is discussed. In terms of therapy, MA has provided an alternative approach for selectively attacking malignant cells. Also discussed is the possibility of linking highly toxic substances to MA for therapy. The use of MA as carriers for chemotherapeutic agents is discussed. This approach to cytotoxic drug therapy is still new and many problems must be resolved. At present, there is as yet no conclusive evidence that the antigens specified by murine monoclonal antibodies on malignant melanoma, osteogenic sarcoma and colorectal carcinoma are recognized by patients. Nevertheless, MA specifying human tumor antigens, are providing new and exciting approaches for biochemically characterizing cell surface proteins and glycolipids. Other possible uses of the new technology are discussed. (97 Refs)

IMMUNOGLOBULIN STRUCTURE AND SYNTHESIS

24. LOCAL IMMUNOGLOBULIN A IN NORMAL AND NEOPLASTIC BREAST TISSUES.

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JNCI; 67(6):1231-1239 1981

Local IgA levels in 36 normal, 92 nonmalignant atypical, and 47 malignant human breast tissue specimens were analyzed by three methods: direct immunofluorescence, modified radioimmunoassay for IgA in cryostat sections, and the Immuno-Fluor (Bio-Rad Laboratories, Richmond, Calif) assay for the cell surface IgA in tissue eluates. The proportion of epithelium in each sample was estimated microscopically. For malignant specimens the proportion of epithelial cells was significantly higher than that for nonmalignant specimens. The immunofluorescence test showed no qualitative difference in epithelial IgA content between normal and nonmalignant atypical tissues, but the frequency of positive specimens were markedly lower in malignant tissues. The modified radioimmunoassay and the Immuno-Fluor assay indicated little or no difference in IgA concentration per tissue wt among normal, nonmalignant atypical, and malignant breast tissues. However, when the data were corrected for proportion of glandular epithelium, nonmalignant atypical tissues had less IgA per cell than normal tissues, and malignant mammary carcinomas had significantly less IgA per cell than both normal and nonmalignant atypical tissues. (Author abstract) (24 Refs)

25. INTRACELLULAR STORAGE OF IGA AND SECRETORY COMPONENT IN CARCINOMAS OF THE FEMALE BREAST.

Syre G, Sehn M
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Virchows Arch [Pathol Anat]; 393(3):315-320 1981

This study reports 10 cases of mammary carcinoma with intracytoplasmic lumina and inclusion bodies visible by light microscopy; five tumors were classified as lobular in type and four as different forms of infiltrating ductular carcinomas. One tumor showed a lobular growth in combination with ductular structures. For the identification of the inclusion bodies, indirect immunofluorescence on paraffin embedded material was performed, which revealed IgA as well as secretory component within the intracytoplasmic lumina. It was concluded that the production of secretory component and the uptake of IgA is possible even in carcinomas without glandular structures, and that immunomorphology should supplement histological and histochemical evaluation in order to define the contents of intracytoplasmic lumina. (Author abstract) (21 Refs)

26. PRODUCTION OF HUMAN IMMUNOGLOBULIN SECRETING CLONES WITHOUT THE USE OF H.A.T SENSITIVE FUSION PARTNERS (MEETING ABSTRACT).

Strelkauskas AJ, Ferrara GB
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Hybridomas and Cellular Immortality (Second Houston Symposium), November 5-6, 1981, Houston, Texas. University of Texas Medical School at Houston 55 pp., 1981.

We have utilized a long term B cell line derived from a patient with acute lymphocytic leukemia as a fusion partner in the production of human hybridoma clones. Our studies center around the production of human monoclonal antibodies to 1) T cell antigens, 2) defined human WBC antigen (HLA) determinants, 3) Rh blood group antigens, and 4) the antigens associated with mammary carcinoma. Fusions are performed using peripheral blood from individuals shown to have an ongoing antibody response to these antigens. Each of the donors is defined with regard to specific HLA type. Twenty-four hr after fusion the cell mixtures are separated using a positive selection technique in which donor cells and clones are sensitized with highly specific human anti-HLA antibodies from planned immunizations, followed by rosetting with red cells coated with purified rabbit anti-human IgG antibodies. Screening for antibody specific HLA determinants was simplified by using cells from donor and recipient couples originally used for planned immunization. Positive results were obtained for anti-Rh antibodies as well as antibodies reactive with mammary carcinoma cell lines and T cell subsets. (no Refs)

27. MONOCLONAL IMMUNOGLOBULINS WITH AFFINITY FOR PLATELETS AND THEIR RELATIONSHIPS TO MALIGNANT LYMPHOMA.

Veenhoven WA, Thomas-van der Schans GS, Nieweg HO
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Cancer; 49(1):40-42 1982

Monoclonal immunoglobulins with affinity for platelets were detected in the blood of seven patients. Two of these had thrombocytopenia and non-Hodgkin's lymphoma (NHL). One patient had thrombocytopenia and possibly incipient NHL. The other four patients had pseudothrombocytopenia at the time of diagnosis but one of them developed NHL 6 years later. It is suggested that these monoclonal immunoglobulins may in some cases be associated with malignant lymphoma and that subjects presenting with these immunoglobulins should have a long term follow-up in order to elucidate the question whether or not lymphoma will develop. (Author abstract) (18 Refs)

28. QUALITATIVE CHARACTERISTICS OF HISTAMINE RELEASE FROM HUMAN BASOPHILS BY COVALENTLY CROSS-LINKED IGE.

Kagey-Sobotka A, Dembo M, Goldstein B, Metzger H, Lichtenstein LM
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J Immunol; 127(6):2285-2291 1981

We have studied the effects of permanent oligomers of human IgE produced using the cross-linking reagent, dimethyl suberimidate, on histamine release from human basophils. IgE dimers were found to be sufficient stimuli for both release and desensitization of these cells; monomeric IgE had no effect. Histamine release was augmented by deuterium oxide (D2O) in the medium, but D2O was not an absolute requirement to observe release. Desensitization by the dimeric IgE was specific in that the response to anti-IgE was not affected by preincubation of the leukocytes with the IgE dimer under suboptimal releasing conditions. IgE trimers and higher oligomers of IgE also caused both release and desensitization. IgE trimers were three- to four-fold more effective than IgE dimers with regard to the amount required for 50% histamine release. Dilution studies with monomeric IgE suggested that the difference was due to the presence of more 'active' dimers in the trimeric IgE fractions. We conclude that dimeric IgE, by juxtaposing two receptors on the basophil membrane, is the 'unit signal' for both release and desensitization of these cells. (Author abstract) (22 Refs)

29. THE CLINICAL ASPECTS OF BICLONAL GAMMOPATHIES: REVIEW OF 57 CASES.

Kyle RA, Robinson RA, Katzmann JA
Mayo Clinic and Mayo Foundation, Rochester, MN, 55905
Am J Med; 71(6):999-1008 1981

Between 1966 and 1979, biclonal gammopathy was recognized in 57 patients. Clinical and laboratory features differentiated three groups: biclonal gammopathy of undetermined significance, 37 cases (65%); multiple myeloma, 9 cases (16%); and lymphoproliferative disease - including lymphoma, macroglobulinemia, chronic lymphocytic leukemia and unclassified lymphoproliferative disorders -11 cases (19%). With biclonal gammopathy of undetermined significance, symptomatic multiple myeloma developed after 2 yr in one patient; the others remained stable. One patient with multiple myeloma had osteosclerotic myeloma and a severe sensorimotor peripheral neuropathy, and another presented with plasma cell leukemia. In the remainder response to therapy and survival were much the same as in patients with multiple myeloma with a monoclonal protein. Patients with lymphoproliferative disease responded to chemotherapy like that for monoclonal gammopathy. Of the 57 patients, 30 (53%) had IgG and IgA components, 15 (26%) had IgG and IgM, 6 had two IgG components, 3 had IgA and IgM, 1 had two IgA proteins, 1 had IgA and IgE and 1 had triclonal gammopathy. Of the 115 light chains, 70% were kappa; the chains were both kappa or both lambda in 63% of biclonal pairs. In many cases, serum electrophoresis produced only a single band on the acetate strip, and the biclonal gammopathy was not recognized until immunoelectrophoresis was done. Although the clinical features of biclonal gammopathy and its response to therapy are similar to those of monoclonal gammopathy, this subject is of importance because of the lack of clinical data in the literature. (Author abstract) (96 Refs)

HUMORAL IMMUNE BLOCKING FACTORS AND ANTIGEN-ANTIBODY COMPLEXES

30. ISOLATION AND ELECTROPHORETIC ANALYSIS OF IMMUNE COMPLEXES FROM PATIENTS WITH BREAST CANCER.

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Lautenberg Center General and Tumor Immunology, Hebrew Univ.-Hadassah Medical Sch., Jerusalem, Israel

Eur J Cancer Clin Oncol; 17(11):1165-1176 1981

Immune complexes (IC) were isolated from sera of patients with breast cancer (BC), from effusions from patients with breast and ovarian cancer (OC) and from effusions from patients with non-malignant diseases. Isolation was carried out with the aid of tubes coated with rheumatoid factor (RF) as immunoadsorbents. The effusions were first filtered through Sephacryl S-300 columns and the large mol wt material eluted in front of the IgG peak was used as the starting material, while most of the sera were processed without prior filtration. The IC eluted from the RF-coated tubes were radioiodinated and analyzed by electrophoresis on polyacrylamide gels, followed by autoradiography. Four putative IC-derived proteins were identified in the RF eluates and designated according to their mol wt (in Kdalton): p94, p46, p17 and p13. Protein94 was found in 1/8 BC effusions, but in none of the other samples tested; 'p46', which was actually a complex of several closely spaced proteins, was identified in at least 3/16 BC sera, 6/8 BC effusions, 3/4 OC effusions and 1/5 non-malignant effusions, but in none of 17 normal sera. The upper band of the complex seemed to be present mainly, if not exclusively, in effusions from patients with neoplasia. Protein17 and p13 were found more often and in higher concentrations in the malignant effusions. All of these proteins could be precipitated by treating the RF eluates with anti human Ig serum, suggesting that they were associated with Ig, presumably as immune complexes. (Author abstract) (35 Refs)

31. IMMUNE COMPLEX-LIKE MATERIALS IN SERA OF PATIENTS WITH BREAST CANCER: DETECTION BY COMPLEMENT-CONSUMPTION ASSAY.

Sulitzeanu D, Asaf O, Biran S, Brufman G, Gilead Z
Lautenberg Center General and Tumor Immunology, Hebrew Univ.-Hadassah Medical Sch., POB 1172, 91120 Jerusalem, Israel
Isr J Med Sci; 17(9/10):869-873 1981

Sera of patients with breast cancer were tested for the presence of immune complexes by a complement-consumption assay. To increase the concentration of immune complexes and thus improve the chances of their detection, sera were first ultracentrifuged and the sedimented material was assayed. Sera were considered to be positive if they consumed at least 75% of the hemolytic activity under the conditions of the test. Of the 60 patients tested, 45% were positive as compared with 13.5% positive sera among healthy blood bank donors. The presence of immune complexes could not be correlated with the extent of disease, the age of the patients, treatment or lack of treatment at the time of the test, or the time that had elapsed since diagnosis. In a few control tests, treatment of samples with DNase had no effect on their anticomplementary activity, whereas reduction with 2-mercaptoethanol abrogated the activity. These results strengthened the assumption that the substances binding complement were indeed immune complexes. (Author abstract) (19 Refs)

32. CIRCULATING IMMUNE COMPLEX AND IMMUNOLOGIC RESPONSES IN PATIENTS WITH MALIGNANT TUMORS.

Saiga T
First Dept. Surgery, Sch. Medicine, Gifu Univ., Tsukasa-cho, Gifu 500, Japan
Nippon Geka Gakkai Zasshi; 82(6):587-598 1981

One hundred forty-four patients with malignant tumors (gastric cancer, 60 patients; colorectal cancer, 42 patients; lung cancer, 32 patients; and breast cancer, 10 patients) were examine d for circulating immune complex (CIC) by C1q solid-phase radioimmunoassay. They were tested for cellular and humoral immunity at the same time and the correlation of the responses with CIC was investigated. Positive CIC was obtained in 16 of the patients (11.1%), a high incidence being noted in patients with advanced cancer. Two of the 13 patients from whom the tumor was not completely removed showed persistent positive CIC postoperatively. The positive rate for delayed skin tests (tuberculin test and phytohemagglutinin response) was higher in patients with positive CIC than in those with negative CIC. No significant difference was observed in the T cell and B cell content between the positive CIC group and the negative CIC group, before or after surgery. Blast formation of lymphocytes showed a tendency to be lower in the positive CIC group than in the negative CIC group, before or after surgery. However, no significant difference was noted. No significant difference was observed in the CH50, C3 and C4 complement systems between the positive and negative CIC groups before surgery. After the operation, the positive CIC group had significantly higher C4 levels than the negative CIC group. No significant difference was observed in serum glycoproteins (alpha1-acid glycoprotein, alpha1-antitrypsin and haptoglobin) between the positive CIC group and the negative group, before or after surgery. Although CIC caused no significant differences in cellular immunity or humoral immunity, it is considered to be a factor which has some influence on them. (48 Refs) (In JPN)

33. IMMUNE IMBALANCE AND IMMUNE MODULATION IN SOLID TUMOR PATIENTS: NEW INSIGHTS.

Serrou B, Cupissol D, Rosenfeld C
Laboratoire d'Immunopharmacologie des Tumeurs, Hopital Saint-Eloi, Centre Paul Lamarque, F-34033 Montpellier Cedex, France
Recent Results Cancer Res; 80:9-16 1982

Immune status in patients with solid tumors is reviewed. Several studies have found a variety of immunocomplexes (IC) that are present in increasing amounts during tumor growth or relapse (TGR) and in decreasing amounts following tumor reduction (TR). Because these complexes are apparently varied and poorly defined, practical use of IC measurements is limited. Changes in the plasma membrane lipid bilayer of WBC occur during TGR and disappear during TR. Plasma microviscosity may change in a similar fashion. Studies of patients treated with BCG have indicated that those with high levels of anti-BCG antibodies generally have a good prognosis, while those with low levels have a poor prognosis. A similar correlation has been found for vitamin A. Vitamin A apparently plays a role in cell differentiation and immune response. The T-gamma lymphocyte/T-mu lymphocyte ratio in patients increases during TGR and decreases during TR. A T-theophylline-resistant lymphocyte population that forms autologous rosettes is reduced during TGR and increases during TR. Suppressor-cell activity is affected by antiprostaglandins or irradiation and has therapeutic implications. Of new immunomodulating drugs, bestatin has antitumor activity in mice and RO-109359 increases cutaneous delayed hypersensitivity; results with interferon are unclear. (28 Refs)

HUMORAL IMMUNOSUPPRESSIVE AGENTS

34. NONSPECIFIC IMMUNOSUPPRESSIVE FACTORS IN MALIGNANT ASCITES: FURTHER CHARACTERIZATION AND POSSIBLE RELATIONSHIP TO ERYTHROCYTE RECEPTORS OF HUMAN PERIPHERAL T CELLS.

Oh SK, Moolten FL

Dept. Microbiology, Boston Univ. Sch. Medicine, Boston, MA, 02118

J Immunol; 127(6):2300-2307 1981

Nonspecific suppressor factor has been purified from malignant human ascites through partial delipidation, ammonium sulfate precipitation, ACA-22 gel filtration followed by goat anti-human IgG immunoadsorbent chromatography. Mol wt estimated by SDS-PAGE under mild reducing conditions is 50,000 and 25,000 under vigorous reducing conditions. It inhibits PHA, Con A, and PWM responses of peripheral lymphocytes by 50% at microgram concentrations per milliliter in vitro and inhibits plaque-forming cell response to SRBC at 100 ug/mouse in vivo. It also inhibits two-way mixed lymphocyte reactions and natural killer cell activities. It inhibits SRBC rosette formation of peripheral T cells and appears to be an erythrocyte receptor of peripheral T cells. (Author abstract) (56 Refs)

35. ANTIGEN-SPECIFIC AND NONSPECIFIC SUPPRESSOR FACTORS DERIVED FROM T CELL HYBRIDOMAS: THEIR FUNCTION AND MOLECULAR ORGANIZATION.

Taniguchi M, Takei I, Saito T, Igarashi M, Karihara K, Tomioka H
Dept. Immunology, Sch. Medicine, Chiba Univ., Chiba, Japan
Int Arch Allergy Appl Immunol; 66(Suppl1):206-211 1981

A study presenting the functional and molecular organization of antigen-specific suppressor factor and some characteristics of I-J bearing antigen-nonspecific suppressor factor is discussed. With the use of the cell hybridization technique, three groups of I-Jb+ T cell hybrid lines with different functional specificities have been established. Some hybrids (34S-18, 34S-704) display an antigen-specific activity, suppressing the IgG response to DNP-KLH (dinitrophenyl-keyhole limpet hemocyanin). Some (34S-44, 34S-15) have an antigen-nonspecific activity, suppressing the IgG response to DNP-egg albumin as well as DNP-KLH. Other cell lines (34S-281, 1L-5), which have I-Jb determinants on their cell surface, showed no suppressive activity. Since suppressive activity was found in the extracted materials of the hybridomas or in the ascitic fluid from the hybridoma-bearing mice, such extracts or ascites were used for further characterization of the antigen-specific or nonspecific suppressor T cell factors (TsF). The studies reported indicate that there are closely linked I-J subregion loci coding for the determinants on the cell surface of different subsets of T cells. Further analysis indicates the possible interrelationships between I-J positive hybridomas. In the authors' laboratory, the acceptor T cell hybridoma after being stimulated by the specific TsF secretes another factor, activating the efferent limbs of the suppressor cell interaction, in which antigen-specific or nonspecific pathways are involved. (23 Refs)

36. IMMUNOSUPPRESSION ASSOCIATED WITH SJL/J MURINE LYMPHOMA. I. SUPPRESSION OF CELL-MEDIATED IMMUNE RESPONSES AFTER TUMOR TRANSPLANTATION.

Kumar RK, Lykke AW, Penny R
Sch. Pathology, Univ. New South Wales, P.O. Box 1, Kensington, New South Wales 2033, Australia
JNCI; 67(6):1269-1275 1981

The proliferative responses of peripheral blood lymphocytes of inbred SJL/J mice to the mitogens phytohemagglutinin and concanavalin A were evaluated serially in individual animals before and after induction of lymphomas by transplantation. Tumor-bearing mice exhibited marked suppression of mitogen responsiveness. Proliferative responses in mixed lymphocyte-tumor cell culture and mixed lymphocyte culture were also suppressed. Suppression of responses was tumor related, and responsiveness was restored in animals whose tumors regressed. There was no deficiency of responder T-cells in the peripheral blood of tumor-bearing animals, and suppressor cell activity was not demonstrable in a number of in vitro assays. However plasma from tumor-bearing animals exhibited potent immunosuppressive activity. The presence of plasma suppressive activity was similarly tumor related. Thus this study demonstrates nonspecific suppression of cell-mediated immune responses following tumor induction, apparently mediated by a plasma suppressor factor. (Author abstract) (35 Refs)

37. IMMUNOSUPPRESSION ASSOCIATED WITH SJL/J MURINE LYMPHOMA. II. CHARACTERIZATION OF A PLASMA SUPPRESSOR FACTOR IN TUMOR-BEARING MICE.

Kumar RK, Lykke AW, Penny R
Sch. Pathology, Univ. New South Wales, P.O. Box 1, Kensington, New South Wales 2033, Australia
JNCI; 67(6):1277-1282 1981

The properties of a factor responsible for immunosuppressive activity in the plasma of inbred SJL/J mice bearing transplanted lymphomas were investigated. Suppressive activity was not due to an intact virus but resided in a soluble molecule characterized as a nonimmunoglobulin protein of mol wt 68,000-88,000. The plasma suppressor factor was relatively stable and was neither directly cytotoxic nor complement-dependent. The degree of suppression of in vitro lymphocyte proliferative responses depended on the time of addition of plasma to cultures. Suppression was reversible if cells exposed to plasma were washed before mitogen stimulation, but stimulated cells exposed to the suppressor factor were irreversibly inhibited. The suppressor factor was partially species-specific. Supernatants from short-term cultures of tumor cells from lymph nodes of SJL/J mice contained a similar suppressor factor, indicating that the plasma factor was probably a product of tumor cells. (Author abstract) (33 Refs)

OTHER RELATED STUDIES

38. A NEW NON-IMMUNOGLOBULIN PRODUCING HUMAN MYELOMA CELL LINE FOR PRODUCTION OF HYBRIDOMAS (MEETING ABSTRACT).

Pickering JW, Gelder FB
Department of Microbiology/Immunology and Surgery, Louisiana State University Medical Center, Shreveport, LA, 71130
Hybridomas and Cellular Immortality (Second Houston Symposium), November 5-6, 1981, Houston, Texas. University of Texas Medical School at Houston 55 pp., 1981.

We selected an 8-azaguanine resistant mutant of a human myeloma cell line (RPMI 8226) by cloning the parental cells on a feeder layer of mouse spleen cells in the presence of increasing concentrations of 8-azaguanine. Culture media and cell-free extracts of both the parental and mutant (8226 AR/NIP4-1) cell lines were assayed for immunoglobulin heavy and light chain by Ouchterlony double immunodiffusion and for lamda chain by radioimmunoassay. Secretion of free lamda chain by the parental cell line was confirmed. In contrast, no immunoglobulin heavy or light chains were detected in culture medium of the mutant cell line by either immunodiffusion or radioimmunoassay. No intracellular lamda chain could be detected in the mutant cells by radioimmunoassay of cell free extracts or by immunofluorescence of fixed cells. Hybridomas were produced by fusion of 8226AR/NIP4-1 cells with lymphocytes from a mesenteric lymph node recovered at surgery from a hypertransfused renal transplant recipient. Twenty hybrid culture media were assayed for immunoglobulin by double immunodiffusion and 15 contained either IgG (lamda) or IgG (kappa). None produced IgM or IgA. One hybridoma producing IgG (kappa) was shown by immunofluorescence not to reexpress lamda chain of the parental myeloma. Hybrid antibodies were screened for reactivity in a lymphocyte microcytotoxicity assay against a panel of 46 normal human donors. One hybrid antibody lysed 50% of peripheral lymphocytes from 4 of the donors. This antibody appeared to recognize an alloantigen present on a subpopulation of human lymphocytes. (no Refs)

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39. HUMAN HYBRIDOMAS (MEETING ABSTRACT).

Croce CM
The Wistar Institute of Anatomy and Biology, 36th Street at Spruce, Philadelphia, PA, 19104
Hybridomas and Cellular Immortality (Second Houston Symposium), November 5-6, 1981, Houston, Texas. University of Texas Medical School at Houston 55 pp., 1981.

Human myeloma cells were mutagenized and selected for deficiency in hypoxanthine phosphoribosyltransferase (HPRT). HPRT deficient mutants were then fused with human lymphocytes derived fr om patients responding to viral antigens and self antigens. Hybridomas secreting anti-viral antibodies and auto-antibodies were obtained. The use of the human hybridoma technology to study human autoimmune diseases will be discussed. (no Refs)

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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HE 20. 3173/2:

TUMOR ANTIBODY PRODUCTION/ CHARACTERIZATION/ DETECTION

1. IMMUNOGLOBULIN- AND ANTIBODY-DETERMINATION OF CHILDREN WITH ACUTE LYMPHATIC LEUKEMIA.

Breitlow D, Schmalz H, Karsch W

Institut fur Infektionskrankheiten im Kindesalter, Stadtischen Klinikum Berlin-Buch, Wiltbergstrasse 50, DDR-1115 Berlin-Buch, E. Germany

Dtsch Gesundheitswes; 36(46):1930-1934 1981

In 30 children suffering from acute lymphatic leukemia the immunoglobulins (Ig) as well as the antibodies (E coli hemagglutination titers) were measured. The data obtained were firstly compared with one another and secondly with the results derived from 144 hospitalized children with mostly acute but generally mild forms of the disease. The Ig levels were lowered (the lowest levels measured in percent were those of IgA). The antibody production measured by the hemagglutination test according to Webster et al was less than that in the 144 control children. Normal E coli hemagglutination titers were found in 13 out of 30 children with leukemia. This proportion appears to be relatively large. There was no correlation between the level of the Ig and that of the E coli hemagglutinin titers. The IgG level was most markedly lowered in recurrent leukemia. A correlation with the duration of disease was indicated only by low E coli hemagglutination titers in the 2nd yr of treatment. It seems likely that patients with low Ig levels but normal E coli hemagglutination titers are better able to combat or control infections than patients with both low Ig levels and low E coli hemagglutination titers. (Author abstract) (27 Refs) (In GER)

2. MONOCLONAL ANTIBODIES AGAINST SURFACE ANTIGENS OF LARYNGEAL CARCINOMA CELLS.

Zenner HP

Universitatsklinik und Poliklinik fur Hals-, Nasen-, und Ohrenkranke, Kopfklinikum Wurzburg, D-8700 Wurzburg, W. Germany

Arch Otorhinolaryngol; 233(2):161-172 1981

Production of monoclonal antibodies against laryngeal carcinoma (LC) cells is reported. BALB/c mice were immunized with LC cells of line HLaC78 (1 x 10(6)-5 x 10(7) cells x 2 at a 6-wk interval) or with cell membranes (CM) from LC cells. Spleen cells were obtained 3 days after the second injection. Spleen cells were fused with mouse myeloma 653 cells to form antibody-producing cells capable of proliferation. A total of 1,882 clones of spleen cells were developed, including 1,102 from mice immunized with CM and 780 from mice immunized with intact cells (IC). Antibodies that bound to intact LC were produced by 73 clones, all from IC-immunized mice. Antibody from one clone was identified which bound malignant target cells, including two types of LC and two types of salivary gland tumor cells, but which did not bind normal fibrocytes, lymphocytes, or other normal human cell types, or nonhuman cells. The antibody, produced by hybridoma clone 1g6, was an IgG. Diagnostic potential of the IgG is described. (32 Refs) (In GER)

3. AMYLASE IN FALLOPIAN TUBE AND SEROUS OVARIAN NEOPLASMS. IMMUNOHISTOCHEMICAL LOCALIZATION.

Bruns DE, Mills SE, Savory J

Dept. Pathology, Univ. Virginia Medical Center, Box 168, Charlottesville, VA, 22908

Arch Pathol Lab Med; 106(1):17-20 1982

We studied the cellular localization of amylase in normal Fallopian tubes and serous ovarian neoplasms using an indirect immunoperoxidase technique. The primary antiserum was against human pancreatic amylase, and was found to inhibit ovarian tumor amylase as well. Amylase was present in normal endosalpingeal epithelium and in the epithelial cells of benign, borderline, and malignant serous ovarian tumors. A mucinous cystadenoma was also studied and contained no amylase. This localization suggests that amylase production by serous ovarian neoplasms reflects the endosalpingeal differentiation of these tumors. Antibody to amylase may be potentially useful in distinguishing serous ovarian tumors from other forms of ovarian neoplasia. (Author abstract) (12 Refs)

4. HUMAN HYBRIDOMAS FROM MALIGNANT GLIOMAS.

Sikora K, Alderson T, Phillips J, Watson JV

Ludwig Inst. Cancer Res., Hills Road, Cambridge, CB2 2QH, England

Lancet; 1(8262):11-14 1982

Intratumoral lymphocytes from 12 patients undergoing craniotomy for malignant glioma were fused with a specially derived human myeloma line LICR-LON-HMy2. Seventy one stable hybridomas were obtained from 5 of the 12 patients. Such hybridomas had a DNA content equal to the sum of that present in lymphocytes and the parent myeloma. The hybridoma supernatants contained human monoclonal immunoglobulins. Glioma-binding activity was detected in 7 out of the 71 supernatants. These results suggest that malignant gliomas contain a population of B lymphocytes which may be involved in host defense against the tumor. (Author abstract) (14 Refs)

5. USE OF CAPILLARY TUBE LEUKOCYTE ADHERENCE INHIBITION FOR THE DETECTION OF TUMOR-SPECIFIC IMMUNE RESPONSE.

Myers WL, O'Keefe ML

Dept. Medical Microbiology and Immunology, Southern Illinois Univ. Sch. Medicine, P.O. Box 3926, Springfield, IL, 62708

Immunol Commun; 10(4):407-416 1981

The tumor-specific immune response of A/J mice was determined at various times after subcutaneous injection with a transplantable spindle-cell sarcoma (SaI) using a leukocyte adherence inhibition (LAI) assay carried out in capillary tubes. Solubilized antigens prepared by 3M KCl extraction of the specific tumor, other transplantable tumors and normal A/J liver were used in the evaluation of LAI reactivity. The assay was found to be capable of detecting a significant antitumor response before the subcutaneous tumors became detectable by palpation. The response remained significant until the tumors were greater than 25 mm in diameter. Responsive cell populations did produce an active supernatant, indicating the possible presence of a lymphokine and/or specific cytophilic antibody. (Author abstract) (19 Refs)

6. CYTOGENETIC STUDIES OF HAIRY CELL LEUKEMIA.

Lele KP, Filippa DA, Chaganti RS
(c/o Chaganti) Lab. Cancer Genetics and Cytogenetics, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York. NY, 10021
Cancer Genet Cytogenet; 4(4):325-330 1981

Mononuclear cells from peripheral blood and spleen of four patients with hairy cell leukemia (HCL) were cultured for 1 to 10 days with and without phytohemagglutinin (PHA) stimulation. Blastogenesis and mitoses were not observed in the unstimulated cells cultured for up to 3 days. Prolonging the culture time of unstimulated cells to 7 days produced blastogenic response; a further increase in culture time to 10 days showed transformed cells but not mitoses. Poor PHA response was noted in the cultures stimulated for 3 days, but cells cultured for 7 days and then stimulated with PHA entered mitosis. Surface immunoglobulins were exhibited in 78-94% of the cells in the blood and spleen of patients. In addition, these cells had tartrate-resistant acid phosphatase and were able to phagocytize latex particles by which properties they were identified as hairy cell leukemia cells. Chromosome abnormalities were present in a proportion of cells of each patient, none of them, however, were clonal. (Author abstract) (12 Refs)

7. MEGAKARYOCYTIC LEUKEMIA: IDENTIFICATION UTILIZING ANTI-FACTOR VIII IMMUNOPEROXIDASE.

Innes DJ, Mills SE, Walker GK
Dept. Pathology, Univ. Virginia Medical Center, Box 214, Charlottesville, VA, 22908
Am J Clin Pathol; 77(1):107-110 1982

Coagulation Factor VIII is produced by endothelial cells and megakaryocytes. Antibody directed against Factor VIII or its associated antigens has been shown to be a sensitive marker for both normal and neoplastic endothelial cells. It use to identify neoplastic megakaryocytes has not been described. We used immunoperoxidase localization of Factor VIII to identify megakaryocytes and immature megakaryocytic precursors in a case of megakaryocytic leukemia. (Author abstract) (14 Refs)

8. IN VIVO RADIOIMMUNODETECTION OF OCCULT RECURRENT COLONIC CARCINOMA.

DeLand FH, Kim EE, Primus FJ, Dine ME, Goldenberg DM
Veterans Admin., Lexington, KY, 40536
AJR; 138(1):145-148 1982

External imaging of radionuclide-labeled antibodies to carcinoembryonic antigen (CEA) was used to detect and localize metastatic carcinoma in a 57-yr-old woman with a rising and markedly elevated plasma CEA level 5 mo after anterior resection of an adenocarcinoma of the sigmoid colon. Other extensive radionuclide evaluations were not helpful in determining the cause plasma CEA elevation. The value of in vivo radioimmunodetection for the demonstration of CEA-containing neoplasms is discussed. (16 Refs)

9. DETECTION OF AN ANTISQUAMOUS ANTIBODY IN MULTIPLE KERATOACANTHOMA.

Ahmed AR, Sofen H, Saxon A
Div. Dermatology, Univ. California Los Angeles Sch. Medicine, CHS 52-121, Los Angeles, CA, 90024
Clin Immunol Immunopathol; 22(1):20-31 1982

A case of multiple keratoacanthoma involving the skin and mucous membranes is reported. An antisquamous antibody was detected in the patient's serum which bound to a membrane antigen on squamous tumor cell lines COLO-16 and SCaBER. The approx mol wt of the antigen is 68,000. The antibody appears to be of the IgG class. It is possible that antibodies such as these may be directed toward neoplastic tissue and could play an important role in spontaneous tumor regression seen in patients with multiple keratoacanthoma. (Author abstract) (32 Refs)

10. A CONTROLLED STUDY OF HEPATITIS CORE ANTIBODY (HBCAB) IN PRIMARY HEPATOCELLULAR CARCINOMA AND LIVER CIRRHOSIS IN KENYA.

Bowry TR, Shah MV, Ahmad Z
Immunology Section, Dept. Human Pathology, Univ. Nairobi, Nairobi, Kenya
East Afr Med J; 58(8):576-582 1981

Incidence of hepatitis B virus (HBV) markers was studied in 75 Kenyan patients with confirmed liver disease. Among these patients, 15 had liver cirrhosis (LC), 13 had LC and concomitant primary hepatocellular carcinoma (PHC), and 47 had PHC. Presence of hepatitis B surface antigen (HBsAg) was detected in 40% of the patients with LC, in 47% of the patients with LC + PHC, and in 46% of the patients with PHC. Among the HBsAg-positive patients, high titers of hepatitis B core antibody (HBcAb) were detected in 100% of the patients with LC, 100% of those with LC + PHC, and 90% of those with PHC. HBcAb as a sole marker of HBV was detected in 13% of the patients with LC, 31% of those with LC + PHC, and 9% of those with PHC. (16 Refs)

11. SPECIFIC, ANTIGENIC PROTEIN OF GUERIN EPITHELIOMA.

Palka JA, Rzeczycki W
Inst. Biochemistry and Medical Analytics, Medical Acad., 15-230 Bialystok 8, Poland
Neoplasma; 28(5):527-532 1981

Specific, antigenic protein of the mol wt 61,000 and 66,000 and isoelectric point 5.15 were isolated from cytosol of Guerin epithelioma and antiserum against these proteins was obtained. These antigens appear to be specific for epithelioma. Such antigens were not found in any normal rat organ. Blood serum of Guerin epithelioma bearing rats does not contain antibodies against these antigens. (Author abstract) (19 Refs)

12. ANTI-POLY(A) POLYMERASE ANTIBODIES IN SERA OF TUMOR-BEARING RATS AND HUMAN CANCER PATIENTS.

Stetler DA, Rose KM, Jacob ST
Dept. Pharmacology and Specialized Cancer Res. Center, Milton S. Hershey Medical Center, Pennsylvania State Univ., Hershey, PA, 17033
Proc Natl Acad Sci USA; 78(12):7732-7736 1981

Poly(A) polymerase (polynucleotide adenylyl-transferase; ATP:polynucleotide adenylyltransferase, EC 2.7.7.12) was covalently linked to diazobenzyloxymethyl-filters and used to screen the sera from a number of tumor-bearing rats and human cancer patients for antibodies to poly(A) polymerase. Sera from rats that had been inoculated with any of several Morris hepatomas or a mammary adenocarcinoma contained immunoglobulins capable of complexing with poly(A) polymerase. No antibodies to the enzyme could be detected in sera from control animals or from those bearing tumors for short periods of time. Antibodies to poly(A) polymerase were also observed in sera from human patients with leukemia, polycythemia vera, and Wilms tumor. The antibodies were not evident in sera from normal volunteers or from patients with nonneoplastic diseases. These included lupus erythematosus, a disorder in which antibodies are produced against an array of nuclear proteins. Immunoglobulins from the serum of one of the human patients were capable of inhibiting poly(A) polymerase activity in vitro, whereas those prepared from the serum of a normal volunteer did not affect enzyme activity. As determined by the diazobenzyloxymethyl-filter technique, the relative concentration of antibodies in the sera of an individual with leukemia (in remission) increased severalfold during a relapse. These data suggest that the presence of antibodies to poly(A) polymerase may be characteristic of sera from cancer patients and that the relative concentration of these antibodies may be indicative of the disease state. (Author abstract) (26 Refs)

13. THE REGULATION OF THE HUMAN ANTITUMOR IMMUNE RESPONSE TO ORGAN-SPECIFIC NEOANTIGENS.

Thomson DM, Phelan K, Scanzano R, Fink A, Bortin MM, Ferrone S, Martin WJ, Pious D
Montreal General Hosp. Res. Inst., Montreal General Hosp., 1650 Cedar Ave., Montreal, Quebec H3G 1A4, Canada
Transplant Proc; 13(4):1952-1954 1981

The mechanism of WBC adherence inhibition (LAI) is discussed. By increasing free intracellular Ca, Ca ionophore and ouabain stimulate a positive response. Lidocaine affects the binding of Ca to membranes and inhibits Ca++ flux; without Ca++ flux, antigen binding does not mediate LAI. Substances that increase intracellular cyclic AMP do not alter an LAI-positive response but convert to positive LAI-negative responses of patients with large tumor burdens. When prostaglandin E2 synthesis is blocked by indomethacin, the response of LAI-positive WBC is unaffected. When the generation of metabolities of the lipoxygenase pathway is blocked, the LAI-positive response is negated. Bridging of cytophilic antibody receptors on membranes of monocytes by tumor antigens is probably transduced into information useful to the cell. The transduction is believed to involve the opening of Ca channels in the cell membrane. Metabolites of the lipoxygenase pathway play an important role in mediating the response to the tumor antigens. Control of the biochemical reaction activated by Ca entry seems to involve intracellular cyclic nucleotide levels. LAI in early cancers is discussed. (13 Refs)

14. IMMUNE RESPONSES IN CARCINOMA OF THE COLON AND RECTUM.

Greco RS
Dept. Surgery, Div. General Surgery, Rutgers Medical Sch., CMDNJ, P.O. Box 101, Piscataway, NJ, 08854
J Med Soc NJ; 79(1):19-22 1982

Cell-mediated immunity (CMI) after surgery in patients with carcinoma of the colon (CC) or rectum (CR) was compared with CMI in normal patients. CMI was measured by leukocyte migration inhibition assays (Lmi) using KCl extracts of tumor tissue. Of forty patients without malignant lesions, infections, or therapy-induced immunosuppression who underwent elective surgery, 27 showed positive Lmi prior to surgery. Of these, 23 showed negative Lmi immediately after surgery; 4 were positive. Lmi turned positive in 10 patients by 30 days after surgery and in 9 patients within 60 days after surgery; Lmi remained negative after 60 days in 4 patients. Patients with CC showed significant positive Lmi against autologous tumor extracts prior to surgery and immediately afterwards. Lmi turned negative during the late postoperative period. Patients with CR showed no significant positive Lmi against autologous tumor extracts at any time. Neither CC nor CR patients showed positive Lmi against allogeneic tumor extracts at any time, suggesting that each tumor was immunologically distinct. Comparison of Lmi in 20 patients undergoing electrocoagulation of CR with Lmi in 20 patients undergoing abdominoperineal or lower anterior resection showed that electrocoagulation had no effect on cellular immunity. Results indicate that surgery and anesthesia have an immunosuppressive effect and that differences in survival between patients with CC and those with CR may be due to differences in immunocompetence. (8 Refs)

15. THE REACTION SPECIFICITY OF VARIOUS MONOCLONAL ANTIBODIES AND CELLULAR ORIGIN AND DIFFERENTIATION OF CULTURED CELL LINES DERIVED FROM HUMAN LEUKEMIAS AND LYMPHOMAS.

Tobinai K, Hirose M, Minato K, Shimoyama M
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Jpn J Clin Oncol; 11(3):469-479 1981

Human hemopoietic tumor-cell lines (6 T-cell; 10 B-cell; 5 non-T, non-B-cell; 2 myeloid; 2 monocytoid) were grown exponentially, and their reactions to 12 monoclonal antibodies (OKT 3, OKT 4, OKT 6, OKT 8, OKI 1, OKM 1, anti-Leu-1, 10.2, (antihuman Lyt 2), 9.6 (antihuman Lyt-3), anti-B1, J5, anti-Mo 1) were evaluated by indirect immunofluorescence assay and by rosette-forming capacity with sheep erythrocytes, human T-lymphocyte antigen, Ia-like antigen, and surface immunoglobulins. The reactivities of the monoclonal antibodies were highly specific against cultured leukemia and lymphoma cell lines, with a few exceptions, which are described. The titer of the antibody differed among the cell lines, indicating that while use of the monoclonal antibodies specific for certain differentiation antigens may be useful for elucidating the cellular origin, stage of differentiation, and subset identification of human hemopoietic tumor cells, the titration of each monoclonal antibody requires the use of several cultured cell lines in order to determine an appropriate concentration for clinical use. (42 Refs)

16. MONOCLONAL ANTIBODIES AGAINST MYCOPLASMA HYORHINIS. A SECONDARY EFFECT OF IMMUNIZATION WITH CULTURED CELLS.

Vennegoor C, Polak-Vogelzang AA, Hekman A
Dept. Immunology, Netherlands Cancer Inst., 1066 CX Amsterdam, The Netherlands
Exp Cell Res; 137(1):89-94 1982

Monoclonal antibodies were prepared against two different human tumor cell lines, the melanoma cell line SK-Mel-25 and the acute lymphoblastic leukemia T cell line CCRF-CEM. Presence of antibodies against human tumor cells in the supernatants of hybridoma cultures was tested by binding of 125I-F(ab')2 anti-mouse IgG. On two occasions a hybridoma culture, initially selected for subsequent cloning as it seemingly produced antibodies against tumor cells, was later found to produce monoclonal antibodies specific for Mycoplasma hyorhinis. In immunofluorescent staining patchy structures were visible which seemed to be attached to the cell surface. By combined staining with FITC-conjugated anti-mouse immunoglobulin for monoclonal antibody, Evans blue for cytoplasm and Hoechst compound number 33258 for DNA, the reaction against mycoplasma could be recognized. These results demonstrate that if cultured cells are used for preparation of monoclonal antibodies, there is a good chance that the selected hybridomas may produce antibodies against 'culture artifacts' such as mycoplasmas, in addition to the target antigens. Thus mycoplasma contamination of cell cultures poses a serious problem in the hybridoma research and the testing system for antibody specificity should be carefully monitored. (Author abstract) (36 Refs)

TUMOR ANTIBODIES ASSOCIATED WITH VIRUSES

17. EXPRESSION OF BOVINE LEUKEMIA VIRUS GENOME IS BLOCKED BY A NONIMMUNOGLOBULIN PROTEIN IN PLASMA FROM INFECTED CATTLE.

Gupta P, Ferrer JF
Cooperative Leukemia Studies Unit, Sch. Veterinary Medicine, Univ. Pennsylvania, Kennett Square, PA, 19348
Science; 215(4531):405-407 1982

Plasma of cattle infected with bovine leukemia virus contains a soluble factor that blocks the expression of the viral genome in cultured lymphocytes. The blocking factor is not present in plasma of bovine leukemia virus-free cattle or of cattle infected with common bovine viruses. Blocking of bovine leukemia virus expression by the plasma factor is reversible, and seems to be mediated by a nonimmunoglobulin protein molecule. (Author abstract) (13 Refs)

18. INHIBITORY EFFECT OF RETINOIDS ON EPSTEIN-BARR VIRUS INDUCTION IN RAJI CELLS.

Zeng Y, Zhou HM, Zu SP
Inst. Virology, Chinese Academy Medical Sciences, Beijing, People's Republic of China
Intervirology; 16(1):29-32 1981

Induction of Epstein-Barr virus (EBV) early antigen after treatment with various combinations of croton oil and n-butyrate was markedely inhibited by retinoids 7901, 7902, Ro 10-9359 and R o 11-1430. Possible administration of retinoids to virus capsid antigen IgA antibody-positive individuals in high-risk areas for nasopharyngeal carcinoma to prevent EBV activation and development of this cancer is discussed. (Author abstract) (12 Refs)

19. GENE PRODUCTS OF MCDONOUGH FELINE SARCOMA VIRUS HAVE AN IN VITRO-ASSOCIATED PROTEIN KINASE THAT PHOSPHORYLATES TYROSINE RESIDUES: LACK OF DETECTION OF THIS ENZYMATIC ACTIVITY IN VIVO.

Barbacid M, Lauver AV
Lab. Cellular and Molecular Biology, NCI, Bethesda, MD, 20205
J Virol; 40(3):812-821 1981

The primary translational product of the McDonough (SM) strain of feline sarcoma virus (FeSV) is a 180,000-dalton molecule, SM P180, that contains the p15-p12-p30 region of the FeLV gag gene-coded precursor protein and a sarcoma virus-specific polypeptide. In addition, cells transformed by SM-FeSV express a 120,000-dalton molecule, SM P120, that is highly related to the non-helper virus domain of SM P180. Both SM-FeSV gene products were found to be intimately associated with the membrane fraction of SM-FeSV-transformed cells. Immunoprecipitates containing SM P180 and SM P120 exhibited a protein kinase activity capable of phosphorylating tyrosine residues of both viral gene products but not immune immunoglobulin G molecules. By independently immunoprecipitating each of the two SM-FeSV proteins we found that most of the tyrosine-specific phosphorylating activity was associated with the SM P120 molecule. In vivo analysis of 32P-labeled SM P180 and SM P120 revealed their phosphoprotein nature; however, both molecules exhibited low levels of phosphorylation and did not contain phosphotyrosine residues. Finally, we did not detect any significant elevation in the levels of phosphotyrosine in the protein fraction of SM-FeSV transformants. Thus, if SM-FeSV were to induce malignant transformation by a mechanism involving phosphorylation of tyrosine residues, the viral gene products must interact with a small subset of cellular proteins that do not represent a significant fraction of the total cellular protein content. (Author abstract) (44 Refs)

20. STRUCTURE AND PHOSPHORYLATION OF THE FUJINAMI SARCOMA VIRUS GENE PRODUCT.

Pawson T, Kung TH, Martin GS
Dept. Microbiology, Univ. British Columbia, Vancounver, British Columbia V6T 1W5, Canada
J Virol; 40(3):665-672 1981

The Fujinami avian sarcoma virus (FSV) transforming gene product, P140, is a fusion protein which contains both gag-related and FSV-specific methionine-containing tryptic peptides. The virion protease p15 cleaved P140 into two fragments: an N-terminal 33K fragment which contained all but one of the gag-related tryptic peptides and a C-terminal 120K fragment which contained all of the FSV-specific tryptic peptides. The 33K gag-related fragment from P140 phosphorylated in FSV-transformed cells contained only phosphoserine, whereas the 120K C-terminal FSV-specific fragment contained both phosphoserine and phosphotyrosine. P140 isolated from cells infected at the nonpermissive temperature with an isolate of FSV which is temperature sensitive for transformation had a normally phosphorylated 33K fragment, but a hypophosphorylated 120K fragment deficient in both phosphotyrosine and phosphoserine. When P140 was immunoprecipitated from cells and phosphorylated in vitro at tyrosine residues in the immune complex kinase reaction, only the FSV-specific fragment was labeled. These data define the structure of FSV P140 and locate the phosphorylated amino acids within the two regions of the polypeptide. (Author abstract) (15 Refs)

21. CHARACTERIZATION OF A BONE MARROW CELL LINE TRANSFORMED BY ABELSON'S MURINE LEUKEMIA VIRUS.

Pinter A, Borzsonyi M
Orszagos Kozegeszsegugyi Intezet, Budapest, Hungary
Magy Onkol; 25(4):217-226 1981

Development of transformed cell line (Gr 17) was observed after infection of a long-term bone marrow cell culture from BALB/c mice with Abelson's murine leukemia virus (strain P 160) (A-MuLV). According to their phenotype, the Gr 17 cells corresponded to the early maturation form of B lymphoid cells (pre-B lymphoblasts). The results of the tests for alpha-naphthylacetate esterase, Hb, phagocytosis, and membrane surface Ig were negative, but cytoplasmic IgM was found. In contrast to the hitherto described cell lines obtained by transformation with A-MuLV, hypodiploid chromosome set and the presence of metacentric chromosome due to translocation were observed. Development of thymus-independent generalized lymphoma was observed after transplantation of Gr 17 cells (2 x 10(7) cells iv) in 4-6-wk-old male and female BALB/c mice. The take rates were 9/10 in the females and 8/10 in the males. The mean latent periods were 41 days in the females and 50 days in the males. Typical Abelson's tumors were induced by the virus produced by the cell line in newborn BALB/c mice. (27 Refs) (In HUN)

22. DETECTION OF THE HUMAN T CELL LYMPHOMA VIRUS P19 IN CELLS OF SOME PATIENTS WITH CUTANEOUS T CELL LYMPHOMA AND LEUKEMIA USING A MONOCLONAL ANTIBODY.

Robert-Guroff M, Ruscetti FW, Posner LE, Poiesz BJ, Gallo RC
Lab. Tumor Cell Biology, NCI, NIH, Bethesda, MD, 20205
J Exp Med; 154(6):1957-1964 1981

The p19 monoclonal antibody for human T cell lymphoma virus (HTLV) and expression of HTLV p19 in cells of patients with leukemia and lymphoma are described. Radioimmune precipitation assay for HTLV proteins demonstrated the specificity of the antibody. Among the iodinated HTLV proteins, only p19 could be specifically precipitated. In indirect immune fluorescence assays, anti-p19 specifically labeled only HTLV-producing cells. Transformed HUT78 cells, derived from a patient with either cutaneous T cell lymphoma or leukemia (CTLC), did not produce HTLV and were negative for p19. Both HUT102 parental cells and clones were 60-70% positive, suggesting that viral expression might be related to cell cycling. CTCL-2 and CTCL-3 cells were 5% and 12% positive, respectively. The fluorescent labeling of virus-positive cells was restricted to the cell membrane. Only fixed cells were labeled, supporting the idea that p19 is an internal HTLV protein and not an envelope component. HTLV p19 is not expressed in most malignant T cells, indicating that replicating HTLV is not present. The monoclonal antibody to HTLV p19 provides an assay of HTLV expression for determining the frequency of HTLV replication in human T cells and for studying the regulation of viral gene expression. (14 Refs)

23. NASOPHARYNGEAL CARCINOMA AND EPSTEIN-BARR VIRUS (EBV)-SPECIFIC IGA.

Desgranges C
Laboratorie d'Epidemiologie et Immunovirologie des Tumeurs CNRS, Faculte de Medecine Alexis Carrel, rue Guillaume-Paradin, 69372 Lyon Cedex 2, France
Pathol Biol (Paris); 29(10):587-589 1981

Studies on EBV-specific IgA in patients with nasopharyngeal carcinoma are reviewed. EBV-specific IgA was found in sera of some subjects in whom nasopharyngeal carcinoma was diagnosed several yr later. Anti-virus capside IgA from the lymphoepithelial mucosa of the nasopharynx can be considered a means of early detection of nasopharyngeal cancer. (18 Refs) (In FRE)

24. HELPER VIRUSES ASSOCIATED WITH AVIAN ACUTE LEUKEMIA VIRUSES INHIBIT THE CELLULAR IMMUNE RESPONSE.

Rup BJ, Hoelzer JD, Bose HR
(c/o Bose) Dept. Microbiology, Univ. Texas, Austin, TX, 78712
Virology; 116(1):61-71 1982

The cellular immune competence of lymphocytes obtained from birds infected with acute or chronic leukemia viruses was studied. The in vitro blastogenic response of thymus-derived lymphocytes (T cells) to the mitogens phytohemagglutinin (PHA) and concanavalin A (Con A) correlates with the ability of birds to elicit a cellular immune response. The PHA response of splenic lymphocytes from birds infected with the avian acute leukemia viruses, myelocytomatosis virus strain 29 (MC29), avian erythroblastosis virus (AEV), avian myeloblastosis virus (AMV), or reticuloendotheliosis virus (REV-T), was completely suppressed within 1 wk after virus infection. The early induction of immunosuppression is therefore a general feature of infection of chickens by avian acute leukemia viruses. Spleen cells from chickens infected with the chronic leukemia viruses, Rous-associated viruses (RAVs) Types 1 and 3, exhibited PHA responses similar to those of uninfected birds. In contrast, lymphocytes from RAV-2 infected birds had suppressed PHA responses. Acute leukemia viruses are replication-defective and are associated with replication-competent nontransforming helper viruses. When chickens were infected with helper viruses isolated from the acute leukemia virus stocks by endpoint dilution, the T-cell response to various T-cell mitogens was completely suppressed. the helper viruses, therefore, contribute to the immunosuppression which occurs during the development of avian acute leukemia. The rapid lethality of the acute leukemia virus could be, in part, the result of the immunosuppressive activity of the associated helper viruses. Though all the acute leukemia viruses severely immunosuppress their hosts, the mechanism by which the immunosuppression was induced by these viruses differed. REV-T was the only acute leukemia virus which induced a population of splenic suppressor cells. All the viruses of the leukosis-sarcoma complex tested which had subgroup B specificity were immunosuppressive while those of subgroup A were not. These results suggest that immunosuppression by these viruses may be related to subgroup specificity. (Author abstract) (49 Refs)

25. EFFECT OF DIFFERENT EPSTEIN-BARR VIRUS-DETERMINED ANTIGENS (EBNA, EA, AND VCA) ON THE LEUKOCYTE MIGRATION OF HEALTHY DONORS AND PATIENTS WITH INFECTIOUS MONONUCLEOSIS AND CERTAIN IMMUNODEFICIENCIES.

Szigeti R, Masucci MG, Henle W, Henle G, Purtilo D, Klein G
Dept. Tumor Biology, Karolinska Institutet, S 104 01 Stockholm, Sweden
Clin Immunol Immunopathol; 22(1):128-138 1982

Leukocytes from healthy Epstein-Barr virus (EBV)-seropositive (SP) subjects show significant migration inhibition (LMI) with EBNA (EBV-determined nuclear antigen)-containing extracts derived from nonproducer, EBV-genome-carrying cells, or presented in the form of partially purified EBNA-preparations. Additional EBV antigens, EA and VCA, presented in the form of induced cell extracts do not add any measurable increase to their response. Leukocytes from acute infectious mononucleosis (IM) patients, on the other hand, do not respond to EBNA, but they show a good response to induced EA- or EA and VCA-containing cell extracts. This is in accordance with known differences in EBV-antibody pattern in healthy SPs as contrasted to acute IM patients. Leukocytes from chronic mononucleosis patients resemble those from acute IM patients in their preferential EA/VCA and deficient EBNA response in the LMI test. Cells from four X-linked lymphoproliferative disease (XLP) patients showed complete absence of reactivity to PHA and to EBV antigens in the LMI test, showing a general defect in cell-mediated immune responses. Leukocytes from a group of patients with lymphoproliferative malignancies in remission and elevated EBV-antibody titers showed a variety of responses, resembling normal SP donors, or IM patients, or showing a complete unresponsiveness in the LMI test. (Author abstract) (41 Refs)

26. HUMAN ANTIBODIES RECOGNIZING THE ENVELOPE GLYCOPROTEIN OF THE BABOON ENDOGENOUS VIRUS BAEV ARE OF HETEROPHIL ORIGIN.

Wernicke D, Kurth R
(c/o Kurth), Paul-Ehrlich-Inst., Frankfurt, W. Germany
Med Microbiol Immunol (Berl); 170(2):135-143 1981

Human sera were tested for antibody reactions against purified envelope glycoprotein from baboon endogenous virus (BaEV). BaEV were produced by culturing in human rhabdomyosarcoma cells and dog thymus cells. Purified viral proteins were labeled with 125I. Sera were obtained from patients with leukemia, lymphoma, teratocarcinoma, or embryonal carcinoma and from normal healthy individuals. None of the sera reacted against the nonglycosylated major core protein p30 from BaEV. All sera reacted against the glycoprotein gp70 from BaEV grown in dog thymus cells (gp70dog) but not to gp70 from BaEV grown in human rhabdomyosarcoma cells. Tests using primarily sera from patients with teratocarcinoma showed that reactivity to gp70dog was blocked by soluble oligosaccharides or animal-cell lysates containing carbohydrates. When gp70dog was enzymatically deglycosylated, human sera no longer reacted. Results indicate that sera from normal individuals and patients with teratocarcinoma contain antibodies that recognize glycoproteins from the envelope of BaEV, and that these antibodies recognize the carbohydrate component of the glycoproteins. The carbohydrate component is apparently coded for by the genome of the host cell. (19 Refs)

ANTITUMOR ACTIVITY AND IMMUNOTHERAPY

27. REJECTION MECHANISMS OF XENOGENEIC TUMOR GRAFT IN THE CHEEK POUCH OF HAMSTER.

Shiraishi M
Dept. Surgery II, Faculty Medicine, Kyushu Univ., Fukuoka 812, Japan
Fukuoka Igaku Zasshi; 72(10):575-588 1981

Rejection of xenografts by hamsters immunized in the cheek pouches with murine tumor cells was studied. Methylcholanthrene-induced tumor cells implanted in the cheek pouches were quickly rejected in immunized hamsters. Cytotoxic activity (CA) was detected by an in vivo neutralization test using cells from immunized hamster but was not detectable by 51Cr-release assay. CA was detected in peritoneal exudate in immunized hamsters bearing peritoneal tumor transplants. A cyclophosphamide- and x-ray-resistant delayed footpad reaction (DFR) was produced soon after immunization. Cytotoxic antibody (CAB) appeared later after immunization than killer activity or DFR. Hamsters exposed to x-rays did not produce CAB but did completely reject tumor xenografts in the cheek pouches. Antibody-dependent cell-mediated CA (ADCC) could not be detectable with antisera from hamsters with increased CA. Results suggest that xenograft rejection is effected by lymphocytes responsible for DFR and cell-mediated CA as detected at the site of rejection; CAB and ADCC apparently play a minor, if any, role in xenograft rejection. (53 Refs) (In JPN)

28. IN VITRO CYTOTOXICITY IN AN IMMUNOLOGIC STUDY OF HUMAN GLIOBLASTOMA.

Parente R, Bucci Sabattini MA, Servadei F
Laboratorio Analisi, Ospedale M. Malpighi, Bologna, Italy
Boll Soc Ital Biol Sper; 57(15):1635-1641 1981

In vitro cytotoxicity (CT) was studied with the aid of cultured tumor cells from histologic specimens of human glioblastomas (GB). The study included 19 patients (30-59 yr old, av age 48 yr, 13 females and 3 males) with GB of Grade III and IV before the start of chemotherapy, 11 healthy controls (HC; 20-35 yr old), and 9 patients with bladder carcinomas (BC). The cells were cultured according to previously published technique and used after one or two transfers. Boyum technique was used for preparation of lymphocytes from fresh, peripheral venous blood. One CT test was mediated by lymphocytes of chronic myelocytic leukemia (CML) according to Cerottini and Engers, and the other was antibody-dependent cell CT (ADCC). Using CML test with lymphocytes from patients with GB, the increase in CT for each group on the av was as follows: GB (37.09 +-3.67%), HC (4.00 +-1.78%), and BC (2.27 +-0.90%). Using CML test with lymphocytes from HC, the following results were obtained: GB (4.90 +-1.51%), HC (2.13 +-0.97%), an BC (1.13 +-0.45%). Using ADCC test with lymphocytes from patients with GB the results were as follows: GB (20.57 +-9.77%), HC (29.18 +-6.67%), and BC (27.66 +-8.51%). CML test indicates activity of NK cells, while ADCC reflects activity of K cells. The difference in results could depend also on inhibitory factors present in serum. (12 Refs) (In ITA)

29. MITOCHONDRIA ARE ASSOCIATED WITH MICROTUBULES AND NOT WITH INTERMEDIATE FILAMENTS IN CULTURED FIBROBLASTS.

Ball EH, Singer SJ
Dept. Biochemistry, Univ. Western Ontario, London, Ontario, Canada
Proc Natl Acad Sci USA; 79(1):123-126 1982

Triple-immunofluorescence experiments with antibodies to cytochrome c oxidase, tubulin and vimentin have been used to immunolabel the mitochondria, microtubules, and intermediate filaments inside the same cultured fibroblasts. In particular, fibroblasts were immunolabeled after they had either been transformed by infection with Rous sarcoma virus or given long-term treatment with cycloheximide. These treatments induced redistribution of the intermediate filaments into a perinuclear arrangement, segregated away from the microtubules, which remained extended to the cell periphery. In such cells, many labeled mitochondria were observed to be codistributed with the peripherally located microtubules. From these results, we infer that an association, probably involving some type of chemical linkage(s), between mitochondria and microtubules exists in these cells that is independent of the intermediate filaments. (Author abstract) (20 Refs)

30. ANTIBODIES AGAINST FELINE AND GIBBON APE REVERSE TRANSCRIPTASE ON SURFACE OF SPLEEN CELLS IN HUMAN MYELOGENOUS LEUKEMIA.

Jacquemin PC
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Eur J Cancer Clin Oncol; 17(12):1283-1286 1981

We reported that antibody bound to blood leukocytes of patients in chronic myelogenous leukemia neutralize reverse transcriptase. The specificity of neutralization depended on the phase of the disease. Antibody bound to chronic phase leukemia cells neutralized Gibbon Ape leukemia virus reverse transcriptase, while that bound to blastic phase cells neutralized Feline leukemia virus reverse transcriptase. Spleen cells obtained from patients with chronic myelogenous leukemia have surface-bound immunoglobulins that recognize both reverse transcriptases. These data in the spleen suggest the existence of a progressive shift in cell population from a chronic phase type cell to a blastic phase type cell. (Author abstract) (9 Refs)

31. ULTRASTRUCTURE AND IMMUNOHISTOCHEMICAL STAINING OF A TRANSPLANTED ENDODERMAL SINUS TUMOR.

Suganuma T, Takao S, Suzuki S, Tsuyama S, Nishi M, Murata F
(c/o Murata) Dept. Anatomy, Kogoshima Univ. Sch. Medicine, Kogoshima 890, Japan
Virchows Arch [Cell Pathol]; 38(2):177-187 1981

An endodermal sinus (yolk sac) tumor was successfully transplanted into athymic nude mice. Histologic and ultrastructural investigations revealed that the transplanted tumor had a characteristic appearance with numerous Shiller-Duval bodies, endodermal sinus structures and ultrastructural profiles as previously described in human material. The endodermal sinus tumor and normal human yolk sac have been found to synthesize not only alpha-fetoprotein (AFP), but also other serum proteins, namely, albumin, prealbumin, alpha1-antitrypsin, and transferrin. Serological study by radioimmunoassay demonstrated AFP, carcinoembryonic antigen (CEA) and human chorionic gonadotropin (HCG) in the sera of the tumor-bearing nude mice and in cyst fluid from the transplanted tumor. Immunohistochemical investigation using the unlabeled antibody peroxidase-antiperoxidase method showed that the tumor cells produced CEA, alpha1-antitrypsin, transferrin, HCG as well as AFP. These immunohistochemical staining properties were correlated with the findings on radioimmunoassay. (Author abstract) (28 Refs)

32. ANTIBODY-DEPENDENT CYTOLYSIS OF THE HUMAN LEUKEMIA CELL LINE K-562 IN THE ABSENCE OF EFFECTOR CELLS OR COMPLEMENT.

Wust CJ, Green M, Lozzio CB, Lozzio BB
Dept. Microbiology, Univ. Tennessee, Knoxville, TN, 37916
Blood; 59(1):133-140 1982

K-562 human leukemia cells grown in the presence of specific goat anti-K-562 gamma globulin, F(ab)'2' Fab', or Fab showed a decrease in DNA and protein syntheses and a loss of cell viability within several hr. Eventually all cells died and lysed within 2-5 days. These events occurred in the absence of added effector cells or complement. The effect on the cell was not due to proteolytic or other external lytic activity generated at the cell surface, since 51Cr-labeled bystander cells or antibody-sensitizer bystander cells (chicken erythrocytes or K-562 cells) were not lysed when added to cultures of K-562 cells incubated with immune globulin. The anti-K-562 gamma globulin was not observed to patch or cap on K-562 cells, but the ability of bound immunoglobulin to fix complement decreased markedly (50% in 60 min), so that no complement-mediated cytolysis could be observed at 2 hr. However, the immunoglobulin, at least portions of it, reacted with fluorescein-labeled rabbit anti-goat gamma globulin for about 16 hr. 125I-labeled immune globulin appeared to be internalized and released into the medium as small degradation products. 125I-labeled Fab did not appear to be internalized, since it was released intact and more rapidly from cells than the intact globulin. (Author abstract) (23 Refs)

33. CHARACTERIZATION OF E-ROSETTE-POSITIVE FC-RECEPTOR-BEARING CELLS BY FLOW CYTOMETRY.

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Dept. Medicine and Pathology, Univ. New Mexico Sch. Medicine, Albuquerque, NM, 87131
Clin Immunol Immunopathol; 22(1):105-117 1982

A subpopulation of human peripheral blood mononuclear cells which have the capacity to form spontaneous rosettes with sheep erythrocytes (E+) have been observed to also express a receptor for the Fc portion of immune complexed IgG. In this study quantitative flow cytometry is used to investigate the binding of human IgG to human E+ cells and to determine the relationship of these IgG-binding cells to the subsets of cells defined by OKT3 and OKM1 monoclonal antibodies. It was observed that a number of E+ cells bear an Fc receptor for monomeric human IgG; that all subclasses of IgG can bind to this subpopulation; that this subset overlaps with the T cell identified with rosetting techniques; and that virtually all of these E+ Fc receptor-positive cells binding monomeric IgG are phenotypically OKM1+ and OKT3-. (Author abstract) (19 Refs)

34. THE PROGNOSTIC VALUE OF IMMUNOFLUORESCENCE FROM ORAL SWABS IN PATIENTS WITH TONSILLAR CARCINOMA.

Mang WL, Hammer C
HNO Universitats-Klinik, Univ. Munich, Ismaningerstrasse 22, 8000 Munchen 80, W. Germany
J Med; 12(6):447-453 1981

Fifty patients with various stages of squamous cell carcinoma of the tonsil were included in the study. All sera of these patients contained antitumor antibodies of the IgG type, which seem to be directed against individual-specific and group-specific tumor cell surface antigen. Different dilutions of autologous antibodies were tested against the tumor specimen as well as against oral swabs taken from the patients after therapy. The autologous antitumor antibodies were visualized on the tumor cell and on the cytology swab by FITC conjugated antibodies from rabbits (anti-human IgG) in the indirect immunofluorescent assay. Although the use of autologous sera avoids the need of absorption, absorption of sera with autologous tumor cells eliminates the reaction completely, with allogenic tumors partially. The prognostic value of humoral immune response in detecting recurrence (immunofluorescence study of oral swabs) is shown by the following observation. After operation swabs taken from the patient's tumor sites are immunofluorescence negative. In case of recurrence, the cells became positive 3-6 mo before local recurrence of the tumor could be clinically detected. (Author abstract) (7 Refs)

35. HETEROGENEITY IN SURFACE ANTIGEN AND GLYCOPROTEIN EXPRESSION OF CELL LINES DERIVED FROM DIFFERENT MELANOMA METASTASES OF THE SAME PATIENT. IMPLICATIONS FOR THE STUDY OF TUMOR ANTIGENS.

Albino AP, Lloyd KO, Houghton AN, Oettgen HF, Old LJ
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
J Exp Med; 154(6):1764-1778 1981

Three melanoma cell lines (DX-1,-2, and-3) derived from separate metastatic foci of patient DX (a 70 yr old woman) were examined for phenotypic differences in growth, morphology, and expression of cell surface antigens and glycoproteins. DX-1 and-2 accumulated visible pigment; DX-3 cell appeared unpigmented. DX-2 and-3 cell lines grew as attached monolayers, while DX-1 showed a marked tendency to grow in suspension after initial attachment as microcolonies of rounded cells. Only DX-1 and-3 cells expressed D-locus human WBC antigen surface antigens. Less marked but characteristic differences were detected in the expression of other cell surface antigens. DX-2 and-3 exhibited similar profiles of cell surface glycoproteins in the high mol wt region, with 90,000 and 120,000 mol wt components being particularly prominent. DX-2 had an additional prominent component of 60,000 mol wt which was only weakly labeled in DX-3. DX-3 exhibited two major glycoproteins in the low mol wt region of 32,000 and 27,000. Only one major glycoprotein of 90,000 mol wt was labeled in DX-1 monolayer cells. Sera from patient DX reacted only with surface antigen of autologous DX-2; the highest reactivity was in the IgG fraction. The time-course of DX autologous reactivity was examined. Absorption analysis indicated that the DX-2 antigen was a class 1 melanoma antigen; the antigen was also detectable in much lower but demonstrable amounts in DX-1 and-3 cells. No other cell type tested exhibited the class 1 DX melanoma antigen. (21 Refs)

36. A MONOCLONAL ANTIBODY THAT DEFINES AN IDIOTOPE WITH TWO SUBSITES IN GALACTAN-BINDING MYELOMA PROTEINS.

Pawlita M, Muschinski E, Feldmann RJ, Potter M
Lab. Cell Biology, NCI, NIH, Betnesda, MD, 20205
J Exp Med; 154(6):1946-1956 1981

The monoclonal antibody HyX24-14 that binds different galactan-binding myeloma proteins (GalBMP) of BALB/c mice with different affinities is described. Amino acid sequence data and hypothetical topographical models were used to partially outline the binding site for the monoclonal antibody on GalBMP. HyX24-14 was derived from an A/J mouse that had been immunized with the X24 GalBMP. Binding affinities were determined for four GalBMP whose variable regions had been completely sequenced; affinity was highest for X24, medium for X44, low for T601, and nondetectable for J539 GalBMP. A structural explanation was proposed for the observed binding activities of HyX24-14. Jk region sequence differences should not directly cause the observed affinity differences because positions 96, 100, and 106 are inaccessible to the surface. Because X24 and T601 have identical L chains up to position 100L, sequence differences in the variable region of the heavy chain and those in the D region are probably responsible for affinity differences. HyX24-14 may interact with a relatively large surface of the GalBMP that includes both parts of CDR-2 and CDR-3 (the D region) of the heavy chain. From molecular models and amino acid sequence data, it is proposed that the idiotope defined by HyX24-14 has two subsites, each of which appears able to bind independently to the antibody. (19 Refs)

37. MODULATION OF NATURAL CYTOTOXICITY BY ALLOANTIBODIES. V. THE MECHANISM OF A SELECTIVE AUGMENTING EFFECT OF ANTI-H-2 ANTISERA ON THE NATURAL KILLER ACTIVITY OF MOUSE SPLEEN CELLS.

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Clinical Immunology Section, Gerontology Res. Center, NIA, NIH, Baltimore, MD, 21224
Cell Immunol; 65(1):115-130 1981

Treatment of mouse spleen cells with specific anti-H-2 antisera augments their natural killer (NK) activity against K562 cells but not against YAC target tumor cells. The same population of natural killer cells was found to lyse K562 as well as YAC target cells, since (a) depletion of YAC reactive NK cells by absorption on YAC monolayers resulted in a concomitant depletion of anti-K562 NK activity of mouse spleen cells, and (b) both K562 and YAC cells could inhibit their own as well as each others lysis in a cross-competition assay. Anti-H-2 antiserum could not induce anti-K562 NK activity in spleen cells previously depleted of NK cells by absorption on YAC monolayers, indicating that alloantiserum does not act by recruiting otherwise nonreactive cells to become cytotoxic toward K562 target cells. In a target-binding assay, K562 binding of NK cells (T-cell, B-cell-, and macrophage-depleted spleen cells) increased five- to eightfold in the presence of anti-H-2 antiserum whereas YAC cells binding of NK cells was not increased. H-2 antigens per se did not appear to be involved in the alloantisera effect since anti-NK antiserum directed against a non-H-2 antigen selectively expressed on NK cells, showed a similar selective NK enhancing effect. Protein A, a reagent which binds to the Fc region of immunoglobulin molecules, completely blocked the alloantiserum induced augmentation of anti-K562 NK activity, but did not alter basal NK activity. Moreover, the F(ab)2 fraction of alloantibodies failed to enhance anti-K562 cytotoxic activity of mouse spleen cells, indicating a crucial role for the Fc portion of the alloantibodies attached to the NK cells, in NK augmentation. Utilization of several target cell lines with or without membrane Fc receptors (FcR) revealed that alloantiserum enhanced the lysis of only FcR+ target cells. It is proposed that alloantibody-coated NK cells, as a result of a secondary interaction between attached alloantibody and Fc receptors on target cells, interact more readily with the target cells and thereby cause a higher level of lytic activity. (Author abstract) (25 Refs)

38. ADCC OF CULTURED HUMAN MELANOMA CELLS: ANALYSIS WITH MONOCLONAL ANTIBODIES TO HUMAN MELANOMA-ASSOCIATED ANTIGENS.

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Scand J Immunol; 14(4):369-377 1981

Four monoclonal antibodies to human melanoma-associated antigens (MAA) were found to be able to mediate specific cell-dependent lysis (ADCC) of cultured human melanoma cells. The extent of specific lysis of melanoma cells was influenced by the effector to target cell ratio, the amount of antibody added to the reaction mixture, and the incubation time. Cultured melanoma cells treated for 16 hr with puromycin or cycloheximide (final concentration, 1.0 ug/ml) displayed increased susceptibility to ADCC even though the cell surface expression of MAA was not changed. On the other hand, treatment of melanoma cells with tunicamycin (final concentration, 1.0 ug/ml) reduced the expression of MAA but did not affect susceptibility to ADCC. These findings suggest that other properties of the target cell membrane besides antigen density play a role in the outcome of ADCC reaction. (Author abstract) (16 Refs)

39. IMMUNOLOGICAL DELINEATION IN NORMAL AND MALIGNANT CELLS OF A MEMBRANE PROTEIN INVOLVED IN GLUCOSE TRANSPORT. II. FUNCTION OF THE ANTIGEN.

Gingrich RD, Wouters M, Bramwell ME, Harris H
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J Cell Sci; 52:121-135 1981

A review of the literature suggested that the antigen detected by the M/27 antibody described in the preceding paper might be involved in the transport of glucose across the cell membrane. This idea was tested by measuring the amount of M/27 antibody bound to cells under a range of conditions known to influence the rate of glucose uptake. Glucose starvation and the administration of insulin under appropriate conditions are known to increase the Vmax for glucose uptake in certain cells, and high cell density in vitro is known to decrease the Vmax. Glucose starvation was found to increase the amount of M/27 antigen present on the surface of two malignant cell lines, but produced no detectable change in five different non-malignant cell types. Insulin increased the amount of M/27 antigen on the surface of both malignant and non-malignant cells. At high cell density, the amount of M/27 antigen present on the cell surface decreased. The changes in the Vmax for glucose uptake produced by these manipulations have been shown not to require the synthesis of protein. This was also found to be true for the changes in M/27 antigen concentration. By disrupting cells in detergent, it could be shown that there was an intracellular pool of M/27 antigen. The total amount of M/27 antigen in the cell was found to be about 4x as large as the amount of the antigen on the cell surface. This figure agrees with the value given in the literature for the size of the intracellular pool of the glucose transport system. The amount of M/27 antigen on the cell surface was found to vary during the cell cycle. A dramatic increase occurred early in S phase. (Author abstract) (31 Refs)

40. MECHANISMS CONTROLLING TCGF PRODUCTION BY CLONED SUBLINES OF EL-4 AZGR IN RESPONSE TO STIMULATION BY ANTI-THY-1 ANTIBODY.

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J Immunol; 128(1):296-301 1982

The effect of xenogeneic anti-Thy-1 antibody on T cell growth factor (TCGF) production by T lymphoma cell lines has been examined as a model system for T cell activation. EL-4 G12 (a cloned subline of the producer EL-4 azgr cell line) produced TCGF when stimulated by a high concentration of anti-Thy-1, but none was induced by low concentrations of anti-Thy-1. Large amounts of TCGF were produced when these cells were cultured with Fc-receptor positive (FcR+) accessory cells. TCGF production by EL-4 G12 showed dose response kinetics similar to TCGF production by anti-Thy-1 stimulated purified normal spleen T cells. Goat anti-rabbit IgG (GaRIG) and Protein A substituted for this accessory helper effect, but neither FcR+ cells nor Protein A worked when (Fab')2 anti-Thy-1 was used instead of IgG anti-Thy-1. Anti-T-200 monoclonal antibody inhibited anti-Thy-1-induced TCGF production by EL-4 G12 and accessory cells. Phorbol myristic acetate and lymphocyte-activating factor also substituted in part for the accessory cell help. The data suggest there are at least two different accessory cell help mechanisms in anti-Thy-1-induced TCGF production, anti-Thy-1-bound membrane aggregation either by GaRIG, Protein A or FcR, and a LAF-dependent mechanism. (Author abstract) (29 Refs)

41. HUMAN CHORIONIC GONADOTROPIN RADIOANTIBODIES IN THE RADIOIMMUNODETECTION OF CANCER AND FOR DISCLOSURE OF OCCULT METASTASES.

Goldenberg DM, Kim EE, DeLand FH
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Proc Natl Acad Sci USA; 78(12):7754-7758 1981

Radioimmunodetection (RaID) of tumors containing human chorionic gonadotropin (hCG; choriogonadotropin) was evaluated in 25 patients by injecting 131I-labeled goat antibody IgG against hCG and performing total-body photoscans with a gamma-scintillation camera 24 and 48 hr later. All 10 testicular cancer patients with proven tumor sites had positive RaID results, whereas three cases without known tumor were negative. Four patients with hydatidiform mole and one with degenerative products of conception showed positive RaID results consistent with elevated serum hCG titers. Two putatively false-positive results were obtained in patients with lung or ovarian cancer, whereas a false-negative metastasis to the liver of a patient with lung cancer and an elevated serum hCG titer was observed. Of 14 tumor sites found by RaID in 10 testicular cancer patients, 4 were revealed by RaID prior to any other detection method used and provided a lead time to definitive diagnosis by other measures of a few days to greater than 1 yr. Although a number of patients had high serum hCG levels, even exceeding 3 ug/ml, the xenogeneic antibody was capable of localizing in tumor. No adverse effects were noted in any of the patients studied. Thus, hCG RaID appears to be a safe and effective method of detecting and locating hCG-producing tumors and has been found to disclose occult testicular cancers. (Author abstract) (26 Refs)

42. IMMUNOLOGICAL DELINEATION IN NORMAL AND MALIGNANT CELLS OF A MEMBRANE PROTEIN INVOLVED IN GLUCOSE TRANSPORT. I. PREPARATION AND PROPERTIES OF THE ANTIBODY.

Gingrich RD, Wouters M, Bramwell ME, Harris H
Sir William Dunn Sch. Pathology, South Parks Road, Oxford OX1 3RE, England
J Cell Sci; 52:99-120 1981

Partially purified preparations of the 200,000 Mr membrane glycoprotein described by Bramwell and Harris were used as antigens to generate monoclonal antibodies. Whether the protein was prepared from human or mouse tumors, the mice immunized with it yielded monoclonal antibodies of broadly similar specificities. All the antibodies obtained were of the immunoglobulin M class, despite a prolonged immunization schedule, and recognized an antigen that was present on the surface of mouse, rat and human cells. One such antibody, M/27, was studied in detail. With the exception of two rat kidney cell lines, the antigen detected by M/27 was found on the surface of all cells grown in culture, whether malignant or not. However, in the mouse, the species in which the antibody was generated, M/27 discriminated sharply between malignant tumors and normal tissues excised directly from the animal. In normal adult or embryonic mouse tissues, whether they were composed of multiplying cells or not, the antigen detected by M/27 was present on the cell surface only at the lower limit of detection, if at all. Malignant mouse tumors grown in the animal produced large amounts of the antigen. Explanation of embryonic mouse fibroblasts induced the expression of the antigen, which was not detected on these same cells in their normal habitat in the growing embryo. Conversely, non-malignant cells that express the antigen in vitro cease to do so when they are re-introduced into the animal. The antigenic determinant appeared to be polypeptide in nature rather than polysaccharide. (Author abstract) (40 Refs)

43. ANTIBODIES IN THE SERA OF PATIENTS WITH BRONCHOGENIC CARCINOMA THAT REACT WITH ANTIGEN FROM A TUMOUR CELL LINE: I. AN ASSAY SYSTEM.

Kelly BS, Stredulinsky V, Vanden Hoek J, Levy JG
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Cancer Immunol Immunother; 12(1):5-10 1981

An antigen prepared from cells of the human squamous cell carcinoma line A549 was tested against human sera from patients with breast, gynecological, and lung cancers, and normal individuals. Altogether 259 serum samples from normal persons and 300 from cancer patients were tried, using an enzyme-linked immunosorbent assay (ELISA). Reactions with antigen were significantly more frequent in sera from all cancer patients and were especially frequent in those with lung cancers including Nelems, squamous cell, adenocarcinoma, untreated oat cell, and oat cell given chemotherapy (17-63%). Samples from patients with other cancers or with lung cancer in remission had less frequent reactions to antigen (0-13%), as did sera from controls (3-7%). A grouping made of 72 sera from patients with lung cancer according to size of lesion yielded the following incidences of abnormal sera: up to 3 cm lesion, 11/72, 3 cm or larger lesion with possible hilar involvement, 13/72, hilar involvement with metastases in the lung area, 25/72, and progressive disease with distal metastases, 22/72. The antigen(s) produced by the A549 line seemed to give a reaction to antibodies of lung cancer patients in the ELISA at many stages of the disease, suggesting that monitoring of patient progress may be possible with this technique. (6 Refs)

44. LYMPHOCYTOTOXIC ANTIBODIES IN CANCER.

Schocket AL, Malesky EV, Kohler PF
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Cancer Immunol Immunother; 12(1):43-47 1981

Cold-reactive lymphocytotoxic antibodies (LCA) were measured in sera from 71 pat ients with various malignancies and 31 healthy controls. Cytotoxicity indices were elevated much more frequently in the sera from lymphoreticular malignancy (LM) patients (10/24) than in the sera from chronic lymphocytic leukemia (0/9), melanoma (5/22), carcinoma (1/16) of the breast, bowel, lung, or uterus patients, or those from normal controls (1/31). In the LM group LCA levels were not correlated with delayed hypersensitivity skin tests, skin croton oil response, total lymphocytes, T cells, or B cells. While LCA is apparently increased in patients with LM, the response is evidently not related to defects in the cell-mediated immune system in some of the patients. (36 Refs)

45. CANCER IMMUNOTHERAPY: SOME CRITICAL COMMENTS REGARDING IMMUNOLOGICAL MONITORING.

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Int J Immunopharmacol; 3(4):339-348 1981

Determination of pretreatment immune status and measurement of drug-related changes in immune response during cancer chemotherapy with levemisole (LV) are discussed. Prior cancer sensitization may be a prerequisite for successful LV treatment and can be determined by various direct and indirect in vivo and in vitro tests. Detection of pretreatment defects in immunologic expression is discussed under the following headings: energy and lymphocytes, monocytes/macrophages, B-lymphocytes, miscellaneous humoral factors, tumor load, suppressor cells, in vitro modulation of functions, and mononuclear cell enumeration. Delayed-type hypersensitivity skin reactions, phytohemagglutinin-induced blast formation, Fe-receptor-bearing lymphocytes, mixed lymphocyte culture reactivity, 'null' cell numbers, and monocyte chemotaxis may show changes during LV therapy and may serve as prognostic indicators. LV may enhance tumor-specific cell-mediated immunity and prolong the presence of high levels of antitumor membrane IgG antibodies in sera of patients receiving tumor vaccines. Exogenous factors that could interfere with desirable immune changes, including surgery, radiotherapy and chemotherapy, are discussed. Timing of LV therapy is discussed in relation to timing of conventional treatment and to the last dose of LV; duration of LV treatment; time as a chronobiological variable; and time as related to delayed-type hypersensitivity skin testing. (57 Refs)

46. ANTI-BROC-A1 (ANTI-H-2S) ANTIBODIES CROSS-REACT WITH HLA-A11.

Ivanyi P, Van Moarik P, De Lange G, Tsuji K, Garrido F, Ferrone S, Oth D, Martin WJ, Festenstein H
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Transplant Proc; 13(4):1958-1961 1981

Antibodies induced by immunization of CBA (H-2k) mice by BROC-A1 (H-2s) ascitic tumor cells were analyzed. The anti-BROC-A1 serum reacted as a k anti-H-2s serum: positive with s, d, q, b, and a haplotypes and negative with k, p, r, and f haplotypes. H-2s cells absorbed all antibody activity, whereas H-2a and H-2b cells absorbed only the cross-reacting antibodies. The results of tests on 121 unrelated Dutch and 70 unrelated Japanese subjects are presented. All A11-positive cells (39) were effectively lysed by the H-2s serum, whereas only 29/152 A11-negative cells were lysed to a comparable degree. The majority of A11-negative cells remained negative with the anti-BROC-A1 serum. Analysis of the HLA profile of A11-negative cells revealed that most cells lysed by higher antibody dilutions bore the antigens B35 and/or B5 in the Dutch panel and B15 in the Japanese panel. Not only H-2s but also the strongly cross-reacting H-2a and H-2b mouse cells could absorb all anti-human activity, suggesting that antigenic factors shared by the specific and cross-reacting targets (public antigens) but not the H-2s haplotype-specific antigens are responsible for the observed cross-reactions of anti-H-2 antibodies with HLA antigens. Strongly positive human cells (A2, A11, B35, B27, C2, C4) could not absorb all (public and private) alloantibodies. (11 Refs)

47. ANTIGENS ON NATURALLY OCCURRING ANIMAL AND HUMAN TUMORS DETECTED BY MONOCLONAL ANTIBODIES.

Embleton MJ, Gunn B, Byers VS, Baldwin RW, Bonavida B, Martin WJ, Ferrone S
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Transplant Proc; 13(4):1966-1969 1981

Reactivities of monoclonal antibodies prepared against a spontaneously arising rat mammary carcinoma and human osteogenic sarcoma cells were studied. An antibody-secreting hybridoma was prepared by fusion of the mouse myeloma P3-

NS1-Ag4 (P3NS1) with spleen cells from rats immunized against a syngeneic mammary carcinoma, Sp4. The monoclonal antibody produced reacted only with mammary carcinoma Sp4 and did not bind to other rat tumors or normal rat cells. Two cell lines (791T/36 and 791T/48) from hybridomas obtained by the fusion of spleen cells from BALB/c mice immunized with the 791T osteogenic sarcoma cell line with P3NS1 cells, produced antibody that reacted preferentially with 791T cells. Antibody 791T/36 reacted strongly with 791T cells and with another osteogenic sarcoma, 788T, and more weakly with two others, 805T and 845T; the antibody did not react with six other osteogenic sarcomas. Tests against 11 lines of cultured fibroblasts, including 3 lines derived from the donor of 791T and 2 from donors of cross-reactive sarcomas, were negative. Monoclonal antibody from 791T/48 gave different cross-reactions. Two different monoclonal antibodies to a human osteogenic sarcoma cell line reacted with the immunizing cell line but not with cultured fibroblasts from the tumor host. Neither showed specificities for blood group or D-locus antigens. Despite apparent tumor association, the antigens detected by the monoclonal antibodies were not shared by all osteogenic sarcomas and were not restricted to this tumor type. (10 Refs)

48. USE OF ANTIBODIES AGAINST TUMOR-ASSOCIATED ANTIGENS FOR CANCER DIAGNOSIS AND TREATMENT.

Ghose T, Ramakrishnan S, Kulkarni P, Blair AH, Vaughan K, Nolido H, Norvell ST, Belitsky P, Bonavida B

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Transplant Proc; 13(4):1970-1972 1981

Antitumor effects of injections of methotrexate (MTX), adriamycin (ADR), and conjugates of MTX and ADR with antitumor globulin (ATG) were determined. Survival of C57BL/6J mice that had received free MTX or MTX conjugated to normal rabbit globulin (NRG) or ATG after ip injection of 10(4) EL4 lymhpoma cells/mouse is described. A dose of 15 mg/kg of free MTX and 3 mg/kg MTX, bound either to NRG or ATG, prolonged survival compared to that of untreated mice. Only MTX linked to ATG produced 'cell cure' in 2/10 mice. Survival of BALB/c mice that received 2 mg/kg of free ADR or 5 mg/kg of ADR linked to normal goat globulin (NGG) or ATG beginning 17 days after inoculation of 10(6) renal carcinoma cells/mouse is described. Although free ADR and ADR conjugated to NGG prolonged the survival of treated mice, only treatment with ADR-ATG conjugates led to long-term survival. When MTX was linked to NRG or ATG, its in vivo toxicity increased and the MTX-ATG conjugate was tumor-inhibitory at dose levels far below equimolar doses of free MTX. When ADR was linked to dextran-IgG, its toxicity was reduced: higher amounts of ADR could therefore be administered without producing a lethal toxic effect. The carrier role of such antitumor antibodies also was supported by the tumor-specific localization of a monoclonal antibody against human melanoma in metastatic lesions. Assay of radioactivity in mice with intracerebral transplants of the C1300 neuroblastoma revealed higher localization by antigen-binding (Fab2) fragments. The results suggested that monoclonal antitumor antibodies and their appropriate fragments are potentially useful for targeting radionuclides and antineoplastic agents. (3 Refs)

49. SPECIFICITY OF SYNGENEIC MONOCLONAL ANTIBODIES AGAINST CELL SURFACE ANTIGENS ON CHEMICALLY INDUCED MOUSE FIBROSARCOMAS.

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Transplant Proc; 13(4):1762-1764 1981

Development and characterization of 16 monoclonal antibodies (McAb) against tumor-specific transplantation antigens (TSTA) are reported. McAb were developed by immunizing C57BL/6 and BALB/c mice with their own syngeneic, chemically induced fibrosarcomas bearing unique TSTA; the formation of hybridomas followed. Radioimmunoessays were carried out with a large panel of normal cells, tumor cel ls, and ecotropic and xenotropic murine leukemia viruses (MuLV). Competitive binding assays used tumor cells and MuLV against well-characterized anti-MuLV gp70 and p15(E) McAb. No highly restrictive tumor specificity was found for any of 16 McAb tested. All McAb showed either MuLV-dependent or MuLV-independent cross-reactivity with several mouse tumor strains. Results obtained with five McAb are tabulated. Reactions to anti-MuLV indicated that M3, PC11, and CS-1 tumor strains express gp70 and p15(E) antigens of ecotropic and/or xenotropic viruses on the cell surface. McAB L1 and 4B1 were specific for tumors bearing MuLV antigens. The 4B1 McAb was specific for a molecule similar or identical to the gp70a epitope of ecotropic MuLV. Three McAb showed tumor reactions independent of MuLV antigens. Failure to produce a tumor-specific McAb may be due to differences in T and B cell function or to sampling luck. (9 Refs)

50. HERITABLE DIFFERENCES AMONG GP70-LIKE MOLECULES ON C3H ULTRAVIOLET LIGHT-INDUCED FIBROSARCOMAS.

Roman JM, Hirsch J, Readhead C, Levy D, DeOgny L, Dreyer WJ, Lennox ES, Rogers MJ, Alexander P, Ferrone S

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Transplant Proc; 13(4):1782-1786 1981

Tumor antigens found on UV-induced fibrosarcomas (UV-FS) in C3H mice were studied. C3H/HeN mice were immunized with UV-FS cells implanted by trocar. Syngeneic antisera (AS) were obtained from the mice. The AS contained antibodies (AB) specific for the immunizing tumor and AB that cross-reacted with other C3H FS lines. Immunoprecipitation of 125I-labeled lysates of six different UV-FS lines detected the consistent presence only of molecules of mol wt 70,000-90,000 dalton. Although resolution of the complexity of the molecules was not possible with one-dimensional gel electrophoresis (GE), two-dimensional GE showed that the tumor molecules recognized by the AS had heterogeneous charges and heterogeneous mol wt. Heterogeneity was possible due to variations in glycosylation, amino acid sequences, or proteolytic processing of precursor molecules. Molecules apparently identical to those precipitated by syngeneic AS were precipitated by goat anti-Rauscher leukemia virus gp70 and goat anti-BALB/c virus-2 gp70 sera. Within a tumor cell line the patterns of heterogeneous molecules in the 70,000-90,000 mol wt range were constant and independent of in vivo or in vitro passage generation. Among various tumor lines considerable variations were apparent. Analysis of molecules from UV-FS suggests that the tumors produce at least two distinct gp70-like molecules, one that is the C3H ecotropic viral gp70 , and one of lower mol wt that is substantially different from ecotropic gp70. (20 Refs)

51. MECHANISM OF THE LOCAL ANTITUMOR ACTION OF INFLAMMATION.

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Transplant Proc; 13(4):1929-1931 1981

Some but not all tumor cells are killed in the environment of a delayed hypersensitivity reaction (DHSR) induced by antigens unrelated to the tumor. Of the several cytotoxic components, cellular and humoral, which are present at the site of a DHSR, a lymphokine released by the interaction of specific antigen with immune T cells--presumptively lymphotoxin--was shown to be responsible for the antitumor action of DHSR. The same mechanism may account for the failure of some tumor cells to grow when inoculated in admixture with BCG. (Author abstract) (7 Refs)

IMMUNOGLOBULIN STRUCTURE AND SYNTHESIS

52. THE NUCLEOTIDE SEQUENCES OF REARRANGED AND GERMLINE IMMUNOGLOBULIN VH GENES OF A MOUSE MYELOMA MC101 AND EVOLUTION OF VH GENES IN MOUSE.

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J Biol Chem; 257(1):277-285 1982

A rearranged variable region (VH) gene of the immunoglobulin heavy chain was isolated as a part of the complete gamma1 chain gene cloned from a phage library containing DNA derived from a mouse myeloma, MC101. A germline counterpart of the VH gene (VH101) was also obtained from a phage library of mouse fetal liver DNA. The complete nucleotide sequences of both rearranged and germline VH101 genes were determined; these sequences indicate that the rearranged VH101 gene comprises three separate germline DNA segments, the germline VH101 gene, a D (diversity) segment, and the J3 segment. The putative transcription initiation site was estimated to be 30 bases 5' to the initiator codon ATG by the determination of the 5'-terminus of the MC101 mRNA. The nucleotide sequences (260 bp) surrounding the transcription initiation site were found to be the same in the germline and rearranged VH101 genes. The nucleotide sequence of the VH101 gene was compared with those of four other VH genes taken from the literature and the evolutionary relationships of these VH genes were examined using the synonymous nucleotide substitutions as a molecular clock. The branching points of the VH genes were estimated to range from 4 to more than 80 million yr ago in the phylogenetic tree. The results indicate that some of the VH gene ancestors evolved in remote time, probably before the diversification of mammalian species, whereas some of the VH genes diverged much more recently. The latter possibility was supported in part by considerable difference in the sizes and numbers of restriction DNA fragments hybridized to the VH101 probe among DNAs of various subspecies of strains of the genus Mus. (Author abstract) (52 Refs)

53. CYTOPLASMIC IMMUNOGLOBULINS IN GIANT LYMPH NODE HYPERPLASIA (CASTELMAN'S TUMOUR) .

Dura WT, Mioduszewska O, Porwit-Ksiazek A

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Virchows Arch [Cell Pathol]; 38(2):239-246 1981

The immunohistologic features were studied in six cases of giant lymph node hyperplasia (GLNH) and the cytoplasmic immunoglobulin (CIg) characteristics were compared with those of follicular lymphoma and nonspecific follicular lymph node hyperplasia. By use of the peroxidase - antiperoxidase (PAP) technique it was shown that GLNH comprised a mosaic, polyclonal population of CIg-producing cells, the CIg pattern being comparable with that observed in follicular lymphadenitis. In contrast, follicular lymphomas disclosed a definite monoclonal pattern, the cytoplasmic Ig containing only one light chain of kappa type. This led to the conclusion that GLNH is not a neoplastic change, but has the characteristics of a reactive process within the B-cell compartment. (Author abstract) (24 Refs)

54. RECOGNITION OF POLYMORHPIC H2 DOMAINS BY T LYMPHOCYTES. I. FUNCTIONAL ROLE OF DIFFERENT H-2 DOMAINS FOR THE GENERATION OF ALLOREACTIVE CYTOTOXIC T LYMPHOCYTES AND DETERMINATION OF PRECURSOR FREQUENCIES.

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J Exp Med; 154(6):1717-1731 1981

The fine specificity and receptor repertoire of cytotoxic T lymphocytes (CTL) was examined. Murine histocompatibility complex (H-2) Kk CTL clones were generated in a limiting dilution system and their fine specificity assessed by target inhibition with a panel of monoclonal (mc) anti-H-2Kk antibodies. Poisson distribution analysis yielded three straight lines, indicating the existence of three precursor populations differing in precursor frequency. Av frequency data were 1/400 for CTL I, 1/2,000 for CTL II, and 1/4,000 for CTL III. Limiting dilution curves suggested that the more frequent CTL populations were subject to a suppressive mechanism. Biphasic curves represented CTL I and II in some experiments and CTL II and III in others. Results of target inhibition studies with a panel of mc anti-H-2Kk antibodies that had previously been shown to define two separate clusters of antigenic determinants on the Kk molecule indicated that CTL subsets differ in their receptor repertoire. Application of a single antibody blocked only a fraction of CTL clones, whereas CTL target interaction was totally prevented when numerous epitopes were covered by a mixture of mc antibody or by an alloantiserum. Each antibody exhibited a characteristic inhibition pattern. Thus, each CTL subpopulation appears to consist of various different clonotypes with specificity for different target epitopes. Generation of CTL subpopulations with specificity for particular domains may be controlled by suppressive mechanisms. The data suggest that CTL recognize basically the same polymorphic domains on the H-2Kk molecule defined by antibodies; regulatory mechanisms apparently determine the expressed repertoire in CTL populations. (25 Refs)

55. THE NATURE OF THE IMMUNOGLOBULIN G ON THE SURFACE OF B LYMPHOCYTES IN CHRONIC LYMPHOCYTIC LEUKEMIA.

Stevenson FK, Hamblin TJ, Stevenson GT
Lymphoma Res. Unit, Tenovus Res. Lab., General Hosp., Southampton, England
J Exp Med; 154(6):1965-1969 1981

Anti-idiotypic antibody was raised against the surface IgM on neoplastic B lymphocytes of five patients with chronic lymphocytic leukemia. Radioimmunoassay of cell lysates indicated that Mu was the predominant heavy chain class for all five patients. This included both surface membrane and intracellular IgM. The levels of IgD and IgG found in lysates were low, with IgG exceeding IgD for all patients. Passage of cell lysates through specific anti-idiotypic immunosorbents resulted in almost complete removal of IgM in all five patients; passage of lysates through control immunosorbents resulted in recovery of 79-123%. Similar results were obtained with IgD, with larger errors due to the small amounts of IgD present. For IgG, however, 81-100% passed through the anti-idiotypic column and 71-100% passed through the control, demonstrating the non-idiotypic nature of the IgG. The majority of all three immunoglobulin (Ig) idiotypes were not retarded when the lysate from the cells of one patient was passed through an immunosorbent carrying anti-idiotype directed against another patient's lymphocytes of the same surface Ig isotype. Thus the IgG frequently found associated with lymphocytes at this stage of differentiation is likely to be extrinsic in origin. (11 Refs)

56. ORGANIZATION AND REORGANIZATION OF IMMUNOGLOBULIN GENES IN A-MULV-TRANSFORMED CELLS: REARRANGEMENT OF HEAVY BUT NOT LIGHT CHAIN GENES.

Alt F, Rosenberg N, Lewis S, Thomas E, Baltimore D
Center Cancer Res., Dept. Biology, Massachusetts Inst. Technology, Cambridge, MA, 02139
Cell; 27(2):381-390 1981

The structure of immunoglobulin-related genes was analyzed in individual Abelson murine leukemia virus (A-MuLV)-transformed lymphoid cell lines. Essentially all of these lines, whether immunoglobulin-containing or null, had DNA rearrangements in the vicinity of the JH regions on both chromosomes as well as deletions of at least 5 kb of DNA 5' to JH. None of these lines, however, except rare light chain producers had detectable rearrangements at either their kappa or lambda light chain loci. In contrast to A-MuLV-transformants derived from bone marrow, those from early fetal liver frequently contained more than 2 and sometimes 12 or more distinct, rearranged JH-containing fragments. Cellular subclones derived from these lines had a subset, usually two, of the fragments found in the parent line. Therefore, heavy chain gene rearrangement appears to precede that of light chain gene rearrangement and is still continuing in certain cultured A-MuLV transformants. (Author abstract) (43 Refs)

57. ANTIBODY DIVERSITY: SOMATIC HYPERMUTATION OF REARRANGED VH GENES.

Kim S, Davis M, Sinn E, Patten P, Hood L
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Cell; 27(3):573-581 1981

The immune response to phosphorylcholine in BALB/c mice has been well characterized. Amino acid sequence analyses of heavy-chain variable (VH) regions from 19 myeloma and hybridoma immunoglobulins binding phosphorylcholine show that 10 are identical (the prototype T15 VH sequence) and 9 are distinct variants differing by one to eight residues. A T15 VH DNA probe was used to isolate four closely related members of the T15 VH gene family, including one encoding the T15 VH sequence, from a sperm genomic library. A comparison of the protein and germline VH sequences suggested that most of the immune response to phosphorylcholine is derived from the T15 germline VH gene segment. The variant heavy chains from the M167 and M603 alpha immunoglobulins differ in their VH protein sequences from T15 by eight and three residues, respectively. We analyzed the somatic variability in and around the coding regions of these two variant VH genes by comparing them with the corresponding regions of the appropriate germline gene segments. The somatic variation has three properties: it is extensive and is found in flanking as well as coding sequences (for example, at least 44 substitutions for the M167 sequence and 10 substitutions for the M603 sequence); in the coding regions, it includes many silent as well as replacement substitutions; and it is focal in nature and centered around the rearranged VH genes. Although the mutations extend into the neighboring upstream and downstream flanking sequences, sequences approx 5 kb upstream and downstream from the VH genes show no substitutions. Moreover, the associated heavy-chain constant genes (Calpha) from both variant alpha genes are unaltered, indicating that a closely linked and coexpressed gene is unmutated. We conclude that this somatic variation is generated by a special hypermutational mechanism highly localized in its site of execution and highly restricted in its time of operation during B-cell development. (Author abstract) (43 Refs)

58. STRUCTURE OF THE HUMAN IMMUNOGLOBULIN MU LOCUS: CHARACTERIZATION OF EMBRYONIC AND REARRANGED J AND D GENES.

Ravetch JV, Siebenlist U, Korsmeyer S, Waldmann T, Leder P
Lab. Molecular Genetics, NIH, Bethesda, MD, 20205
Cell; 27(3):583-591 1981

The variable portion of an immunoglobulin heavy chain gene is assembled from at least three discontinuous segments of DNA, the V, D and J regions. We have characterized a 30 kb segment of the human genome that plays a critical role in the formation of this variable region as well as in the expression of the two heavy chains that appear earlier in immunocyte ontogeny, the mu and delta chains. This region encodes nine J-like segments, an interspersed D segment, recombination signals and the genes responsible for the production of both mu and delta heavy chains. Six of the nine germline J-like genes appear to be active and easily account for most of the known human heavy chain amino acid sequences. Three of the J-like genes are pseudogenes. The large number of human J region genes and, hence, their greater potential for generating diversity as compared to that of the mouse J region genes appears to result from recent genetic duplications. To assess this potential, we have analyzed two recombinant genes involving this region. One of these, a V-D-J recombinant, is likely to be an active gene; the other, an aberrant D-J recombinant. A comparison of the structures of these D regions raises the possibility that they are mosaics formed by recombination between D segments. (Author abstract) (37 Refs)

59. A CROSS-REACTIVE IDIOTYPE, QUPC52 IDX, PRESENT ON MOST BUT NOT ALL ANTI-ALPHA(1-6) DEXTRAN-SPECIFIC IGM AND IGA HYBRIDOMA ANTIBODIES WITH COMBINING SITES OF DIFFERENT SIZES.

Sharon J, D'Hoostelaere L, Potter M, Kabat EA, Morrison SL
Dept. Microbiology, Columbia Univ. Coll. of Physicians and Surgeons, New York, NY, 10032
J Immunol; 128(1):498-500 1982

Seven BALB/c IgM, 4 BALB/c IgA, and 1 C57BL/6 IgA anti-alpha(1-6) dextran hybridoma antibodies were characterized idiotypically. Five of the seven IgM and all four BALB/c IgA proteins bear a cross-reactive idiotype present on the anti-alpha(1-6) dextran BALB/c myeloma protein QUPC52 and on a majority of anti-alpha(1-6) dextran antibodies in BALB/c mice. Of these nine monoclonal antibodies, some have combining sites as large as six glucose residues, and some have combining sites as large as seven glucose residues. Individual idiotypes present on QUPC52 are differentially expressed on the nine hybridoma proteins that bear the cross-reactive idiotype. One BALB/c IgM hybridoma protein and the C57BL/6 IgA hybridoma protein did not react with anti-QUPC52 idiotypic antibodies; another BALB/c IgM hybridoma antibody showed only marginal reactivity. (Author abstract) (21 Refs)

60. CYTOLOGICAL CHANGES OF THE CONJUNCTIVA IN IMMUNOGLOBULIN-PRODUCING DYSCRASIAS.

Spinak M, Jakobiec FA
111 E. 210th St., Bronx, NY, 10467
Ophthalmology (Rochester); 88(12):1207-1211 1981

Fifteen patients (7 women, 63-72 yr old; 7 men, 51-78 yr old; 1 other) were selected randomly from patients with documented immunoglobulin-producing dyscrasias. Of patients with normal-appearing conjunctivae, 10/13 exhibited abnormal epithelial cells in cytologic preparations made from scraping. These abnormalities consisted of rouleaux-like formations plus scattered islands of epithelial cells resembling rosettes or giant multinucleate cells. Cells from one patient had immunoglobulin inclusions (Dutcher bodies) and epithelial cell hypertrophy. Others had giant cells and intermediate-appearing cells with PAS-positive granules. The results may indicate immunoglobulin-producing dyscrasias which should be further studied by serum electrophoresis. An accompanying discussion questions the cytological description and appraisal of the evidence; lack of data on the chemotherapeutic histories of the patients, which might affect cytological evaluation, is criticized. The presence of Dutcher bodies is not considered sufficient to indicate systemic disease in the present cases. (19 Refs)

61. IG BIOSYNTHESIS IN A HUMAN PRE-B CELL LINE.

McCune JM, Fu SM
Rockefeller Univ., 1230 York Ave., New York, NY, 10021
J Immunol; 127(6):2609-2611 1981

Ig synthesis was investigated in a human Epstein-Barr virus transformed pre-B-like lymphoblastoid line, Josh 4. Translation of total extracted cellular RNA in a wheat germ cellfree system showed that the transcripts for both mum (the heavy chain of membrane IgM) and mus (the heavy chain of secreted IgM) were present in approximately equal proportions. Pulse-labeling of cells with 35S-methionine in culture followed by immunoprecipitation and endo-N-acetylglucosaminidase digestion of the precipitates demonstrated that each of these chains were synthesized and glycosylated intracellularly. No light chain synthesis was detected in either system. In addition, both mu-chains were found to be degraded before transit to the plasma membrane or to be secreted. Hybrids formed between Josh 4 and two light chain-producing lymphoblastoid lines, RPMI-8866P (IgGkappa) and 32a1 (IgAlambda), were found to express surface IgM. Thus the provision of light chains permitted membrane expression of chains which might otherwise be degraded. These findings were discussed in relation to normal B cell development. (Author abstract) (20 Refs)

62. TUMOR IMMUNITY TO MURINE PLASMA CELL TUMORS. VII. EXPRESSION OF H-2 AND TUMOR ANTIGENS ON IG SYNTHESIS VARIANTS OF MPC-11.

Giorgi JV, Burton RC, Scott D, Warner NL
Transplantation Unit, Dept. Surgery, Massachusetts General Hosp., Boston, MA
Int J Cancer; 29(1):119-126 1982

As a part of our continuing investigations directed toward defining the nature of the antigens on murine plasmacytomas (PCT), MPC-11 and two immunoglobulin (Ig) synthesis variants of this cell line were examined for H-2 and tumor-associated antigen (TAA) expression, and for the possible role of H-2 in the cytotoxic T lymphocyte response to TAA. The tumor lines studied were MPC-11 (an IgG2b producer), MPC-11.662 (a variant which produces only light chains), and NP.2 (a variant which produces neither Ig chain). Both H-2 expression, which was analyzed by flow cytometry and by cold target cell blocking of the activity of cytotoxic T lymphocytes (CTL) generated in allogeneic cultures, and TAA expression, which was analyzed by cold target cell blocking of the activity of tumor-specific CTL generated in syngeneic cultures, were found to be quantitatively similar on the three lines. When a possible association between H-2 and TAA expression was examined by testing the ability of anti-H-2 sera to block tumor-specific CTL directed against MPC-11, no association between H-2 and TAA was detected. The results of these studies provide new information about H-2 and TAA expression on murine PCT. Furthermore, they suggest that changes in H-2 and TAA expression which have been reported to sometimes accompany loss of Ig synthesis may represent independent genetic, phenotypic, or metabolic variations, rather than alterations linked to the loss of Ig synthesis. In addition, these results, in agreement with our previous studies on MPC-11, support the concept that there is not an obligatory association of TAA with H-2 on the surface of murine PCT. Because these results differ from those reported in some other systems in which an association between H-2 and TAA on murine PCT was demonstrated, it must be emphasized that the TAA of PCT appear to be quite heterogeneous, and more investigations will be necessary in order to clearly define these antigens and the T-cell response to each of them. (Author abstract) (41 Refs)

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HUMORAL IMMUNE BLOCKING FACTORS AND ANTIGEN-ANTIBODY COMPLEXES

63. ACTIVATION OF FC RECEPTOR-BEARING LYMPHOCYTES BY IMMUNE COMPLEXES. II. KILLER LYMPHOCYTES MEDIATE FC LIGAND-INDUCED LYMPHOKINE PRODUCTION.

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Dept. Pediatrics, Temple Univ. Sch. Medicine, Philadelphia, PA, 19133

J Exp Med; 154(6):1868-1880 1981

The roles of the constant fragment (Fc) portion of IgG (Fc gamma) and of the Fc gamma receptors (FcR) in immune complex-induced lymphokine production (ICLP) were studied. Nonadherent lymphocytes enriched 3-to 4-fold in killer (K) cells and in other Fc gamma-binding cells showed antibody-dependent cellular cytotoxicity (ADCC) at approx 1/10 of the lymphocyte:target ratios required for unfractionated nonadherent lymphocytes. These K-cell enriched lymphocytes were induced by chicken antibody-sensitized RBC (EA), by aggregated human gamma globulin (AgHGG), or by sensitized P815 mouse mastocytoma cells to produce lymphocyte migration-inhibiting factor (LIF) at approx 1/10 of the concentration necessary for production of similar levels of activity by unfractionated cells. K cell but not natural killer (NK) cell depletion virtually eliminated ADCC and ICLP. K cells incubated with antibody-sensitized glutaraldehyde-treated P815 cells produced high levels of LIF in the supernatant; NK cells yielded little or no LIF activity when incubated with or without AgHGG. Isolated Fc gamma fragments stimulated nonadherent lymphocytes to produce high levels of LIF activity. Fc gamma fragments did not inhibit WBC migration but blocked EA-rosette formation by lymphocytes. Binding of Fc gamma ligands to FcR of the appropriate lymphocytes was the only requirement for ICLP. (49 Refs)

64. DEFINITION AND CLASSIFICATION OF TROPHOBLASTIC DISEASE BASED ON ITS NATURE.

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Dept. Obstetrics, Niigata Univ. Sch. Medicine, Niigata, Japan

Excerpta Med Int Congr Ser; 551:413-417 1981

Gestational trophoblastic disease (GTD) includes hydatidiform mole (HM), invasive mole (IM), and choriocarcinoma (CCA). HM may be a missed abortion with growing trophoblast. This is supported by evidence that the demise of the embryo may proceed before the formation of HM. Ultrasonic findings associated with defective gestation include poorly defined gestational sac, absence of fetal echoes, failure of growth of the gestational sac in spontaneous abortion, and a snowstorm shadow at high amplification. The production of blocking antibody is regulated mainly by antigenic capacity, especially in expression of Human leukocyte antigen-D determinants of the conceptus that is the embryo-trophoblast unit. IM is a HM in which villous trophoblast invades the myometrium without cellular changes. CCA is a malignant disease in which tumor is made up mainly of trophoblasts that are totally lacking any residual villous structure. (15 Refs)

65. INDUCTION OF IMMUNE CYTOLYSIS: TUMOR-CELL KILLING BY COMPLEMENT IS INITIATED BY COVALENT COMPLEX OF MONOCLONAL ANTIBODY AND STABLE C3/C5 CONVERTASE.

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Dept. Molecular Immunology, Res. Ins. Scripps Clinic, La Jolla, CA, 92037

Proc Natl Acad Sci USA; 78(12):7707-7711 1981

The unique specificity of monoclonal antibodies (Ab) was combined with the cell-killing function of the cytolytic alternative pathway of complement. The functionally C3b-like glycoprotein of cobra venom was linked to a murine monoclonal Ab directed to a human melanoma-associated antigen by a disulfide bond, by using a heterobifunctional crosslinking reagent. The covalent monoclonal Ab-cobra venom factor (CVF) complex exhibited specific cytolytic activity in the presence of normal or C4-deficient serum. It induced killing of melanoma cells but not of LG-2 lymphoblastoid cells or P815 mastocytoma cells. The cytolytic action of the monoclonal Ab-CVF complex was selective in that it was limited to the melanoma cells when these were mixed with one of the two other cell lines. In absence of serum, the complex was noncytotoxic. Monoclonal Ab or CVF alone had no cytolytic activity with or without serum. It is concluded that CVF covalently linked to melanoma cell-bound Ab forms the stable C3/C5 convertase with factors B and D of the alternative pathway, which in turn causes formation of the membrane attack complex and thereby cell death. (Author abstract) (32 Refs)

66. ALTERED SURFACE CHARACTERISTICS OF LYMPHOCYTES FROM PATIENTS HAVING ORAL CARCINOMA.

Vijayakumar T

Regional Cancer Center, Medical Coll., Trivandrum 695011, Kerala, India

Indian J Cancer; 18(4):268-270 1981

The homing patterns of purified lymphocytes of oral cancer patients were compared to those of lymphocytes obtained from healthy controls. Lymphocytes from both groups were isolated and tagged with 51 Chromium in vitro, then injected into mice. Four hr later, radioactivity in liver and spleen was determined and compared. The homing pattern of lymphocytes obtained from oral cancer patients was drastically different from that of lymphocytes obtained from controls. The ratio of radioactivity in the liver/spleen of controls was 31.5:1, while that of oral cancer patients was 10.5:1. These differences could be eliminated if lymphocytes from cancer patients were incubated at 37 C for 24 hr, presumably destroying a cell surface abnormality. These results are compatible with the presence of circulating antigens or antigen-antibody complexes in the peripheral blood of cancer patients. (6 Refs)

67. INVESTIGATION OF IMMUNOGLOBULINS, CIRCULATING IMMUNE COMPLEXES AND PLASMA FREE HEMOGLOBIN IN CANCER PATIENTS ON 60CO GAMMA-RAY THERAPY.

Horvath M, Rode IL, Fekete B, Kiss B, Ringwald G
Natl. Inst. Oncology, P.O. Box 21.1525, Budapest, Hungary
Strahlentherapie; 157(10):673-676 1981

Thirty-two patients with different tumors were irradiated by 60Co gamma-rays. During therapy lasting for several weeks, changes in the content of immunoglobulin and of some other serum proteins, circulating immune complexes and plasma free hemoglobin were determined. Immunosuppression according to immunoglobulin content in serum was not produced by this type of radiation. Decrease in immune complex levels was a good prognostic sign. Low values of plasma hemoglobin content during treatment indicated that no erythrocyte membrane damage had been effected. (Author abstract) (11 Refs)

68. IMMUNE COMPLEXES AND HUMAN NEOPLASIA. DETECTION AND QUANTITATION OF CIRCULATING IMMUNE COMPLEXES BY THE FETAL LIVER CELL ASSAY.

Salinas FA, Wee KH, Silver HK
Cancer Control Agency British Columbia, 2656 Heather St., Vancouver V52 3J3, Canada
Cancer Immunol Immunother; 12(1):11-19 1981

Mouse fetal liver cells (FLC) were used in development of a radioimmunoassay (RIA) for circulating immune complexes (CIC). The uptake of 125I-antihuman IgG by FLC preincubated with sera from patients with various disorders was used to quantitate CIC. Results from unfractionated aggregated human gamma globulin (AHG) and aggregates of defined size were higher with the FLC-RIA than with the Raji assay. FLC-RIA revealed elevated CIC in cancer patients as follows: malignant melanoma, 64/76, breast carcinoma, 38/77, ovarian carcinoma, 40/86, lung carcinoma, 5/17, colon carcinoma, 9/12, and testicular carcinoma, 3/4. The FLC/RIA and Rai tests were compared using 70 serum samples; results were generally in agreement, but FLC-RIA was more sensitive in quantitation of CIC for fewer and smaller immune complexes, conditions in which the Raji assay is reportedly relatively insensitive. (50 Refs)

69. CORRELATION OF CIRCULATING IMMUNE COMPLEXES AND DISEASE STATUS IN PATIENTS WITH LEUKAEMIA.

Hubbard RA, Aggio MC, Lozzio BB, Wust CJ
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Clin Exp Immunol; 43(1):46-53 1981

The occurrence of soluble immune complexes (IC) was investigated in 177 serum samples from 92 patients with various leukemias using the Raji cell immunoassay. In general, patients with myeloproliferative diseases had a higher incidence and higher quantities of IC than did patients with lymphoproliferative disorders. Elevated levels of IC were found in the sera of patients as follows: 17% with chronic lymphocytic leukemia (mean value of 13.1 ug/ml), 67% with acute lymphocytic leukemia (54.1 ug/ml), 65% with chronic myelocytic leukemia (86.7 ug/ml), 70% with acute myelocytic leukemia (202.5 ug/ml) and 56% with acute myelomonocytic leukemia (41.9 ug/ml). Patients in terminal blastic crisis of chronic myelocytic leukemia had the highest levels, with a mean level of 1,364.1 ug/ml. Serial samples were obtained, as available, from individual patients during the course of the disease in an attempt to relate severity with the incidence and quantity of IC. No significant correlation could be made between the occurrence or levels of IC and the presence or absence of systemic symptoms. Similarly, no correlations could be made between levels of IC and hematological parameters, infection, or therapy. However, the data does indicate a positive relationship between the levels of IC and the progressive state of the leukemia, especially, the myelocytic leukemias. (Author abstract) (27 Refs)

HUMORAL IMMUNOSUPPRESSIVE AGENTS

70. CHARACTERISTICS OF BK PAPOVAVIRUS DNA PREPARED DIRECTLY FROM HUMAN URINE.

Mew RT, Lecatsas G, Prozesky OW, Harley EH
(c/o Harley) Dept. Chemical Pathology, Univ. Cape Town Medical Sch., Observatory 7925, South Africa
Intervirology; 16(1):14-19 1981

DNA was prepared directly from preparations of papovavirus excreted in the urine of two patients on immunosuppressive therapy, without preliminary amplification in cell cultures. EcoRI, BamHI, and HindIII restriction patterns were typical of BK virus DNA and were identical for the two isolates. However, there were significant differences in the sizes of the HindIII fragments when compared with those of standard cell-culture-adapted BK virus strains. (Author abstract) (13 Refs)

71. HUMORAL IMMUNITY AND HUMORAL IMMUNOSUPPRESSIVE FACTORS IN HYPOPLASTIC LEUKEMIA.

Ishitani K
Fourth Dept. Internal Medicine, Sapporo Medical Coll., Sapporo, Japan
Rinsho Ketsueki; 22(6):801-804 1981

Levels of each class of serum immunoglobulin in nine patients with atypical leukemia (AT) were compared with those observed in overt leukemia. Levels of gamma globulin, IgG, IgA, and IgE were normal in AT patients. Serum blocking factors, as determined by measurement of alpha-2-macroglobulin and alpha-1-antitrypsin, showed unique fluctuations during the course of AT. It was suggested that serum immunosuppressive factors may be useful in the evaluation of immune status in patients with atypical leukemia. (8 Refs) (In JPN)

72. INHIBITORY EFFECT OF BOVINE SEMINAL RIBONUCLEASE ON ACTIVATED LYMPHOCYTE LYMPHOBLASTOID CELL LINES IN VITRO.

Soucek J, Matousek J, Chudomel V, Lindnerova G
Inst. Haematology and Blood Transfusion, 128 20 Praha, Czechoslovakia
Folia Biol (Praha); 27(5):334-345 1981

The effects of bovine seminal ribonuclease (AS RNase) and its four modified derivatives on pokeweed mitogen (PWM)-stimulated human lymphocytes, on mixed lymphocyte cultures, and on growth of four lymphoblastoid cell lines were examined. Native AS RNase, isolated as a dimer from bovine seminal vesical fluid, was used to prepare the carboxymethylated, succinylated, oxidized, and reduced forms of the enzyme. Native AS RNase exerted the strongest suppressive effect on phytohemagglutinin (PHA)-, PWM-, and mixed lymphocyte reaction-stimulated lymphocytes. At 5 and 100 ug/ml, AS RNase inhibited lymphocyte stimulation by 40 and 95%, respectively. The inhibitory effect persisted in the presence of a 20-fold increase in PHA. Simultaneous addition of AS RNase and (3H)thymidine to transformed lymphocytes did not affect thymidine uptake. AS RNase also had the strongest inhibitory effect on growth, viability, and DNA in the four lymphoblastoid lines tested. AS RNase decreased DNA synthesis in Molt-3 and UHKT-2 cells, with a decrease in live cell count compared to controls. Immunosuppressive effects of AS RNase suggest that the compound is one component of seminal plasma which may take part in suppression of immune responses of the female reproductive tract to spermatozoa. (21 Refs)

73. IMMUNOSUPPRESSIVE ACTIVITY OF THE SERUM IN PATIENTS WITH BRAIN TUMORS AND VARIOUS NEUROLOGICAL DISORDERS: ANTI-SHEEP RED BLOOD CELL PLAQUE-FORMING CELL RESPONSE IN MOUSE SPLEENS.

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Dept. Neurosurgery, Kyoto Univ. Medical Sch., Kyoto, Japan

Nippon Geka Hokan; 50(6):796-808 1981

Immunosuppressive activity (IA) in sera from patients with brain tumors or other neurological disorders was studied using anti-sheep RBC plaque-forming cell response in C3H/He mouse spleens. Immunosuppression occurred more often among patients with glioblastoma (26/30 cases), meningiomas (26/30 cases), other brain tumors (10/14 cases), or non-neoplastic disorders (23 of 30) than among normal individuals (2 of 26). The only correlation found between IA and other immunological parameters was an increased rate of negative results (80%) for purified protein derivative skin tests. Among brain tumor patients IA increased in proportion to the size of the lesion as measured by computed tomography. IA in serum from healthy individuals was increased by reducing the amount of serum injected into mice from 0.4 ml to 0.04 ml; IA in serum from patients with brain tumors or other neurological disorders was reduced by a similar dose reduction. Mixing 0.4 ml of normal serum with 0.4 ml of serum from patients with brain tumors eliminated IA, suggesting that normal serum contains immunosuppressive and immunoenhancing factors, and that the immunoenhancing factors are selectively reduced in patients with brain tumors. Because IA could not be transferred consistently by injection of spleen cells, IA is apparently mediated by a mechanism other than suppressor cells generated in the spleen. (50 Refs) (In JPN)

74. ASSOCIATION OF IMPAIRED IMMUNE RESPONSIVENESS OF LYMPHOCYTES FROM ANIMALS BEARING LARGE TUMORS WITH A MEMBRANE-BOUND SUPPRESSIVE SUBSTANCE.

Wang BS, Heacock EH, Onikul SR, Chang-xue Z, Young TH, Mannick JA

Chemotherapy Res. Dept., Lederle Lab., The American Cyanamid Co., Pearl River, NY, 10965

Cancer Res; 42(2):416-420 1982

The immunoreactivity of lymphocytes from mice bearing large tumors was investigated. As compared to normal lymphocytes, lymphocytes from tumor bearers manifested a lessened proliferative response to T-cell mitogens and were less capable of destroying syngeneic tumor target cells. However, the impaired reactivity of these lymphocytes was improved significantly after washing repeatedly in tissue culture medium in vitro. The increase in cytolytic activity was tumor specific. A membrane-associated suppressive substance was detected in the washing medium which inhibited the cytotoxicity of washed lymphocytes. The effect of suppressive substance was tumor specific and sensitive to treatment with protein A and anti-immunoglobulin antibody, indicating that the suppressive substance contained immunoglobulin. The present findings suggest that a membrane-associated suppressive substance(s) may be in part responsible for the diminished immune responsiveness of lymphocytes from animals bearing large tumors. (Author abstract) (23 Refs)

75. SELECTIVITY IN THE EFFECTS OF INDOMETHACIN ON BCG-ACTIVATED SUPPRESSOR CELL POPULATIONS.

Bennett JA, Kemp JD, Mitchell MS, Rao VS

Dept. Surgery, Albany Medical Coll. of Union Univ., ME Building 514, Albany, NY, 12208

J Immunopharmacol; 3(2):221-239 1981

Indomethacin (IND) and the related compounds salicylate (salicylic acid), aspirin, and RO3-1314 were tested on BCG-induced macrophage-like suppressor cells from the spleen (S) and their precursors from the bone marrow (BM) of female C57BL/6 mice. In vitro immunization of S cells with irradiated P815 mastocytoma was prevented by pretreatment of S donor mice with BCG. All four drugs, when added at the initiation of coculture, almost completely blocked the inhibition of immunization produced by BCG-stimulated cells. IND was most effective: it was inactive at concentrations less than 10(-7) M while at concentrations greater than 10(-5) M it was itself immunosuppresive. Exposure to IND throughout the immunization culture period was more effective in blocking suppressor cells than shorter exposure, and the later IND was added the less was its blocking effect. The inhibitory activity of BCG-induced splenic suppressor cells was primarily in the nylon wool-adherent cells; IND inhibited suppressor activity in both adherent cells and unfractionated S cells. BM cells from BCG-treated mice were twice as suppressive as those from normal mice, but IND was not as effective in blocking the suppressor effect as it was with S cells. Nylon wool-adherent BM cells were more immunosuppressive than nonadherent cells; cells from both normal and BCG-treated mice suppressed immunization of normal cells. Immunosuppressive ability of adherent BM cells from both normal and BCG-treated mice was partially blocked by IND. While suppression generated by nonadherent marrow from normal mice was partially blocked by IND, it was ineffective on BM cells from BCG-treated mice. (37 Refs)

OTHER RELATED STUDIES

76. FUNCTIONAL CHANGES OF MACROPHAGES FROM POLYOMA TUMOR-BEARING MICE.

Pituch-Noworolska A, Pajdak E

Div. Clinical Immunology and Microbiology, Inst. Pediatrics, Wielicka 265, 30-663 Krakow, Poland

Arch Immunol Ther Exp (Warsz); 29(4):423-429 1981

CBA mice were inoculated with different doses of polyoma tumor cells. The PHA response of spleen cells from tumor-bearers was decreased but the spontaneous incorporation of 3H-leucine was increased. PHA-induced cytotoxicity of spleen cells was increased only in tumor-bearers. The expression of Fc receptors showed a slight increase on adherent cells from spleen and peripheral blood mononuclear cells under suboptimal conditions for EA rosette formation (small amount of antibody for coating the erythrocytes). The non-specific esterase activity was assayed in an extract of peritoneal macrophages and the elevated activity with isoenzymes was seen in a group of tumor-bearers. The results suggest a functiona l alteration of macrophages in polyoma tumor-bearing mice. (Author abstract) (24 Refs)

77. BIPHASIC PATTERN OF BACTERIAL INFECTION IN MULTIPLE MYELOMA.

Savage DG, Lindenbaum J, Garrett TJ
(c/o Lindenbaum) Dept. Medicine, Harlem Hosp. Center, New York, NY, 10037
Ann Intern Med; 96(1):47-50 1982

Since the 1960s, gram-negative bacilli have become commoner pathogens than Streptococcus pneumoniae in multiple myeloma. To investigate this trend, we analyzed 75 bacterial infections in 57 patients with myeloma. Episodes of infection with Streptococcus pneumoniae and Hemophilus influenzae occurred at presentation, early in the disease, and in patients responding to chemotherapy. Gram-negative bacilli and Staphylococcus aureus caused 80% of infections seen after diagnosis and 92% of deaths from infection. Episodes of infection with gram-negative bacteria occurred in patients with active and advancing disease and in those responding to chemotherapy when neutropenic. Impaired antibody production may be the major immune defect leading to S pneumoniae and H influenzae infections whereas some additional factor or factors related to disease activity appear to predispose to gram-negative infection in myeloma. (Author abstract) (30 Refs)

78. RED CELL IMMUNE ADHERENCE (RCIA): ITS APPLICATION IN CANCER AND AUTOIMMUNE DISEASE.

Siegel I, Gleicher N
Dept. Obstretrics and Gynecology, Div. Reproductive Immunology, Mount Sinai Sch. Medicine, One Gustave L. Levy Place, New York, NY, 10029
Immunol Commun; 10(4/5):433-449 1981

A rosette technique is described which measures the relative activity of the red cell immune adherence (RCIA) receptor. Antibody-coated sheep red cells, in the presence of complement, adhere to human red cells and thus form mixed human-sheep red cell aggregates (RR-rosettes). The percentage of human red cells adhering to one or more sheep red cells is used as the parameter of RCIA activity. The RCIA receptor activities of 23 cancer patients, 13 patients with autoimmune diseases, and 39 age-matched controls were compared by investigating the ability of human red cells to adhere to antibody and complement coated sheep red cells and thus form RR-rosettes. We noticed a decrease in the percentage of RR-rosette forming cells in cancer patients (p less than 0.0005). In contrast, patients with autoimmune disease showed a significant increase in RR-rosettes when compared to age-matched controls (p less than 0.05). Thus malignancy and autoimmune disease are associated with surface changes of erythrocytes, specifically those of the receptors, which are responsible for the immune adherence reaction. (Author abstract) (21 Refs)

79. EFFECT OF IRON DEFICIENCY ON TRANSPLANTABLE MURINE PLASMACYTOMA.

Benbassat J, Hershko C, Laskov R, Eliakim M
Dept. Medicine A, Hadassah Univ. Hosp., P.O. Box 12000, Jerusalem, Israel
Nutr Cancer; 3(1):20-26 1981

The effect of iron deficiency on tumor growth and host survival was studied in BALB/c mice with transplanted Plasma Cell-II tumors. Each experiment consisted of 60-120 mice into three groups: Group A was maintained on a commercial Purina diet; Group B received a diet of 50% milk powder and 45% corn flour supplemented with 5% oil and 1 mg CuCl2/100 g diet; Group C received the Group B diet supplemented with 200 mg FeCl3/100 g diet. Iron deprivation retarded the growth of weanling BALB/c mice but had no significant effect on the body wt of adult BALB/c mice. Well-formed tumor masses were palpable in greater than 90% of the animals at the site of inoculation within 20 days after injection of 4 x 10(6) tumor cells, and within 35 days after injection of 10(6) tumor cells. In most iron-deficient weanlings, the implanted tumors showed no increase in size from day 25 after inoculation. Iron deprivation of adult mice had no effect on tumor size. The survival of hosts fed on the Purina diet (Group A) was significantly shorter than that of iron-deficient tumor-bearing animals. No significant differences were noted in survival between iron-deficient tumor-bearing mice (Group B) and mice maintained on the same diet with iron supplementation (Group C). (22 Refs)

80. GAMMA (IMMUNE) INTERFERON PRODUCTION BY LEUKOCYTES FROM A PATIENT WITH A TG CELL PROLIFERATIVE DISEASE.

Hooks JJ, Haynes BF, Detrick-Hooks B, Diehl LF, Gerrard TL, Fauci AS
NIDR, NIH, Building 10, Room 2B19, Bethesda, MD, 20205
Blood; 59(1):198-201 1982

We report a patient with a disease characterized by proliferation of T cells with Fc receptors for IgG (TG). However, unlike lymphoid cells from normal individuals or from patients with other lymphoid malignancies, the patient's lymphocytes spontaneously produced gamma interferon (IFN-gamma) in vitro. The peripheral lymphocytes consisted of 95% TG cells, which exhibited the morphological characteristics of T-cell chronic lymphocytic leukemia (CLL) and were normal on cytochemical and chromosome analysis. The majority of TG cells were OKT3+, OKT8+, and OKT4-, 3A1-. These cells failed to express suppressor cell activity and displayed depressed levels of natural killer activity, but mediated antibody-dependent cell-mediated cytotoxicity. The spontaneous production of IFN-gamma by human peripheral lymphoid cells as demonstrated in this study may serve as a probe for studying the relationship between IFN-gamma and the proliferation of human T-cell subsets. (Author abstract) (16 Refs)

81. ADHERENT IA+ MURINE TUMOR LINES WITH CHARACTERISTICS OF DENDRITIC CELLS. I. MORPHOLOGY, SURFACE PHENOTYPE, AND INDUCTION OF SYNGENEIC MIXED LYMPHOCYTE REACTIONS.

Cohen DA, Kaplan AM
Dept. Surgery, MCV/VCU Cancer Center, Medical Coll. Virginia, Virginia Commonwea lth Univ., Richmond, VA, 23298
J Exp Med; 154(6):1881-1896 1981

Several adherent cell lines cloned from mouse P388 leukemia were isolated and characterized. The cell lines were morphologically and functionally similar to dendritic cells (DC) of the spleen with respect to dendritic processes, large numbers of mitochondria, surface expression of immune region-associated (Ia) antigens, and induction of syngeneic and allogeneic mixed lymphocyte reactions. Of adherent P388 cells, 24-69% were positive for Ia antigen, greater than 95% were positive for major histocompatibility D, splenic macrophage-associated, and T cell-associated antigens, and 0% were positive for surface immunoglobulins; positive values were obtained in 13-42%, greater than 95 %, 0, greater than 95%, and 0%, respectively, of nonadherent cells. Both adherent and nonadherent forms of P388 expressed Ia antigens, with a broad range of fluorescent intensity within each respective clone. Cell-to-cell variability of surface Ia antigens in both adherent and nonadherent cells was also detectable with antisera against I-A subregion antigens. Adherent cells strongly stimulated syngeneic and allogeneic T lymphocyte proliferation in the absence of antigen; cytotoxic T cells directed against the stimulators were induced only during allogeneic stimulation. Nonadherent P388 clones did not stimulate either allogeneic or syngeneic T cell proliferation. (28 Refs)

82. ROLE OF CELLULAR IMMUNITY IN RELATION TO SPECIFIC HEMATOLOGICAL FEATURES IN TYPICAL LEUKEMIA.

Takahashi T, Nakayama S, Hoshino T

Second Dept. Internal Medicine, Kyoto Univ., Kyoto, Japan

Rinsho Ketsueki; 22(6):792-800 1981

The role of immunocompetent cells in the development of unusual and unique hematological features of atypical leukemia was studied. A well-preserved hypersensitivity reaction to recall antigen was demonstrated by a higher rate of positive tuberculin tests than in overt leukemia. Despite lymphocytopenia, circulating lymphocytes exhibited normal proportions of T cell subsets and normal phytomitogen responsiveness. Residual physiological suppressor cells were observed. Suppressor lymphocytes were induced in response to various types of immunologic stimulation, including blood transfusion: co-cultured patient circulating lymphocytes suppressed growth of allogeneic normal culture colony forming units (CFU-C) and pokeweed mitogen-induced immunoglobulin production of allogeneic normal lymphocytes. An intercellular control mechanism between immunocompetent cells and a leukemia clone of atypical leukemia was suggested by the suppression of abnormal CFU-C colony and cluster formations by co-cultured autologous T-cells. Atypical leukemia cells showed persistent natural killer effector activity. (13 Refs) (In JPN)

83. OPSONIC ACTIVITY OF MYELOMA IMMUNOGLOBULINS (MM-IG).

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Div. Hematology-Oncology, Univ. Utah Medical Center, Salt Lake City, UT, 84132

Am J Hematol; 11(4):347-353 1981

Patients with MM are at an increased risk for life-threatening bacterial infections, primarily by organisms that require opsonization for interaction with granulocytes. In the present study we used a neutrophil chemiluminescence (CL) assay of opsonization to explore the opsonic activity of MM-Ig for zymosan particles. Particles were treated with serum lacking in Ig to explore the contribution of Ig to zymosan opsonization. This serum was found to have 69 +-2.6% (chi square +- SEM) of the opsonic activity of normal serum (p less than .001). Normal serum concentrations of normal IgG, MM-IgG, and MM-IgA all lacked opsonic activity for zymosan. However, when particles were treated with Nl-IgG, MM-IgG, or MM-IgA as well as complement, normal opsonic activity was generated. Increasing the concentration of the Ig to stimulate MM serum did not inhibit this opsonic activity. Thus both MM-IgG and MM-IgA can function as normal, nonspecific opsonins. (Author abstract) (35 Refs)

84. TWO SEPARATE GENES REGULATE SELF-IA AND CARRIER RECOGNITION IN H-2-RESTRICTED HELPER FACTORS SECRETED BY HYBRIDOMA CELLS.

Lonai P, Bitton S, Savelkoul HF, Puri J, Hammerling GJ

Dept. Chemical Immunology, Weizmann Inst. Science, Rehovot 76100, Israel

J Exp Med; 154(6):1910-1921 1981

Four H-2 heterologous T cell hybridoma clones were used to study the genetic control of dual and anti-nominal antigen and anti-self major histocompatibility complex (H-2) specificity of H-2-restricted T cell factors. The hybridomas were derived from the fusion of BW-5147 lymphoma cells and anti-(4-hydroxy-5-iodo-3-nitrophenyl)acetyl-chicken gamma globulin (NIP-CGG)-primed C57BL/6 splenic cells. Each cell line produced two separate H-2-restricted helper factors. One of them expressed the anti-self specificity of the normal T cell partner (H-2b) of the hybridoma, whereas the other expressed that of the BW-5147 lymphoma cell (H-2k). The restriction appeared to map to the left side of the H-2 complex. Both constant fragment (Ia)b- and Iak-bearing factors were present in the culture fluid of the T77-146-C3 clone, suggesting that the clone secretes two H-2-restricted helper factors, one specific for chicken gamma globulin (CGG)+H-2b and the other for CGG+H-2k. When examined for helper activity, 6/9 clones and subclones were active in helping both H-2b/d and H-2k/d B cell sources. Both helper factors contained similar heavy chain variable region determinants. All five hybridoma clones and subclones tested expressed antigens controlled by both the k and b allele of H-2K and H-2D. T86 clones expressed fewer H-2 antigens than T77-146 subclones. The results suggested that dual specificity is due to two independent loci and suppo rt the validity of dual recognition concepts. Anti-self specificity was associated with homologous Ia alloantigens in the individual factors, suggesting that Ia and anti-self may be linked. (28 Refs)

85. INFLUENCE OF IN VITRO IRRADIATION UPON LIF PRODUCTION BY CONA STIMULATED MONONUCLEAR CELLS.

Sandru G, Veraguth P

Lab. Radiobiology, Dept. Radiotherapy, Univ. Berne, Inselspital, 3010 Berne, Switzerland

Int J Radiat Oncol Biol Phys; 7(12):1679-1683 1981

The effect of in vitro irradiation on production of leukocyte migration inhibitory factor (LIF) by lymphocytes stimulated with Concanavalin A (ConA) was studied. Human mononuclear cells (MNC) from healthy individuals were cultured with or without 90 min pulse exposure to 80 ug ConA/ml. MNC cultures were exposed to irradiation (150 to 1,200 rads within 30 min) before or after exposure to ConA. Irradiation before or after ConA stimulation did not impair LIF production compared to that of non-irradiated MNC. Irradiation produced moderate but significant increases in LIF production in some cultures, mainly those from donors showing poor LIF release after ConA stimulation. MNC culture supernatants that were pretreated with rabbit anti-LIF antibodies had no inhibitory effect on migration of human granulocytes or guinea pig peritoneal exudate cells, indicating the specificity of LIF. Radioresistance of LIF stimulation suggests that LIF production does not require cell proliferation. The increase of LIF production in irradiated MNC cultures suggests that a suppressor-cell population exists that is radiosensitive. Results of the study have implications for immune changes in patients undergoing radiotherapy. (28 Refs)

86. DECREASED TUMORIGENICITY OF RODENT CELLS AFTER FUSION WITH LEUKOCYTES FROM NORMAL AND LEUKEMIC DONORS.

Geurts van Kessel AH, De Boer WC, Van Agthoven AJ, Hagemeijer A
Dept. Cell Biology and Genetics, Erasmus Univ., Rotterdam, The Netherlands
Somatic Cell Genet; 7(6):645-656 1981

Hybrid cell lines, derived from fusion of tumorigenic rodent cells (mouse Pg 19 or Chinese hamster a3) with WBC from leukemic donors were isolated and tested for growth in congenitally athymic nude mice. Cytogenetic analysis, using banding techniques, was performed on cells before injection and on the tumors which eventually developed. Pg 19 mouse cells alone were highly tumorigenic; 1 x 10(5) cells resulted in 100% tumors. The a3 grew more slowly and 2 x 10(6) cells were needed to produce tumors in 75% of mice in 10 days. WBC from chronic myeloid leukemia donors, with inocula of up to 4 x 10(7) cells, failed to form tumors within 3 mo in nude mice, further immunosuppressed by ip cyclophosphamide. The chromosome analyses did not reveal a human chromosome-bearing factor(s) which singly appeared responsible for the tumor suppression. The presence of the Philadelphia translocation in the leukemic cells does not appear to have deprived these cells of their tumor-suppressing ability. (29 Refs)

87. EA-ROSETTE TEST IN CERVICAL CELL SUSPENSIONS.

Noltenius H, Bergmann R
AK St. Georg, Lohmühlenstrasse 5, D-2000 Hamburg 1, W. Germany
Anal Quant Cytol; 3(4):281-284 1981

The erythrocyte-antibody (EA)-rosette test (RT), which detects constant fragment receptor-bearing cells within a cervical population, was studied as a potential screening technic for the early detection of cervical cancer. Of cervical suspensions from 2,437 patients, 54% had a negative RT: no EA-rosette-forming cells (ERFC) were observed. Forty-six percent had a positive RT test: one or more rosettes were observed. Comparison with conventional cytology showed that cytologically positive cases, containing severely dysplastic and carcinomatous cells, were 98.3% EA-rosette positive; only 1.7% were EA-rosette-negative. A cytologic preparation of ERFC from a cervical cell suspension is presented. The presence of ERFC cannot be predicted from the number of inflammatory cells seen in the conventional cytologic smear: cervical cell populations with numerous inflammatory cells may or may not contain ERFC. Three false negatives were reported, two in patients whose cytologic finding of severe dysplasia was confirmed histologically as carcinoma in situ. One patient with a false-negative RT had an invasive carcinoma that had been previously irradiated. Results suggest that the RT might decrease the necessity for cytologic screening and decrease the percentage of false-negative results in cytologic screening. (1 Ref)

88. IMMUNOGLOBULIN EXPRESSION BY HUMAN B LYMPHOCYTES CLONALLY TRANSFORMED BY EPSTEIN BARR VIRUS.

Brown NA, Miller G
Dept. Pediatrics, Yale Univ. Sch. Medicine, New Haven, CT, 06510
J Immunol; 128(1):24-29 1982

Epstein Barr virus (EBV) immortalizes human B lymphocytes, resulting in long-term lymphoblastoid cell lines. To date, such cell lines have typically been derived by suspension culture of mixed mononuclear cells, infected in vivo or in vitro with EBV. We have derived 208 lymphoblastoid lines by clonal transformation of peripheral blood lymphocytes from three neonates, three normal adults, and one patient with systemic lupus erythematosus (SLE), utilizing colony formation in agarose and then separate propagation of the colonies in liquid medium. A total of 180 lines have been analyzed for expression of cytoplasmic and/or secreted immunoglobulin isotypes. Such analysis reveals that 167 (92%) of the lines are monoclonal with respect to isotype expression. All clonally derived lines from neonates produce only IgM. Most clonal transformants from normal adults also produce IgM (81%), but clones producing IgG (16%) or IgA (3%) were also found. Clonal transformation of lymphocytes from the SLE patient revealed a shift in isotype expression, with increased numbers of IgG-secreting clones (48%) and IgA-secreting clones (13%). The data support the use of EBV-mediated clonal transformation as a probe for the analysis of states of isotype differentiation among circulating B cells, and as a method for deriving immortalized, monoclonal human B cell lines. (Author abstract) (34 Refs)

89. HUMAN T CELL SUBPOPULATIONS DEFINED BY A MONOCLONAL ANTIBODY. II. EVIDENCE FOR CELL COOPERATION IN THE RESPONSE TO ALLOANTIGENS AND GENERATION OF CYTOLYTIC CELLS.

Moretta A, Corte G, Mingari MC, Moretta L
Lausanne Branch, Ludwig Inst. Cancer Res., Epalinges, Switzerland
J Immunol; 128(1):20-23 1982

It has been shown previously that the 5/9 monoclonal antibody defines a small T cell subpopulation in human peripheral blood that includes all the cells responsible for proliferation to tetanus toxoid and to alloantigens as well as the helper cells for B cell differentiation. In the present study, human peripheral blood T cells were fractionated according to their reactivity with the 5/9 monoclonal antibody and stimulated in mixed lymphocyte culture (MLC). In spite of a strong proliferative response in MLC, 5/9+ cells generated no cytolytic activity against PHA-activated lymphocytes bearing the stimulating alloantigens (CTL activity) or against the K562 human cell line (NK activity). The precursors of these cytolytic effector cells were present in the 5/9-fraction. However, 5/9+ cells or soluble factors derived from 5/9+ cells were needed to induce 5/9-cells to respond in MLC and develop cytolytic activity. Both 5/9+ and 5/9-cell populations, upon MLC stimulation, were able to lyse L1210 mouse lymphoma cells in the presence of specific antibodies (ADCC). (Author abstract) (16 Refs)

90. DECREASED LEVELS OF CIRCULATING LYTIC ANTI-T IN THE SERUM OF PATIENTS WITH METASTATIC GASTROINTESTINAL CANCER: A CORRELATION WITH DISEASE BURDEN.

Bray J, Maclean GD, Dusel FJ, McPherson TA
Dept. Medicine, Cross Cancer Inst., 11560 University Ave., Edmonton, Alberta, T6G 1Z2, Canada
Clin Exp Immunol; 47(1):176-182 1982

Using a cytotoxicity assay, we have shown that all of 40 normal human sera tested contained antibodies cytotoxic for neuraminidase-treated red blood cells in the presence of complement. The antibodies were shown to be specific for the T disaccharide by studies using a synthetic T antigen. Certain patients with metastatic gastrointestinal cancer were found to have depressed serum levels of anti-T when compared to normal controls. There was a correlation between depression of circulating anti-T and disease burden in that 83% of patients with extensive disease had lower than normal levels of cytotoxic anti-T as compared to 45% of patients with moderate disease and none with minimal disease. There was no corre lation between the concentration of cytotoxic anti-T and the age of the patients, time since surgery or the type of therapy the patient was receiving. Patients with low levels of cytotoxic anti-T had normal levels of cytotoxic anti-sheep red blood cell antibody. Measurement of circulating anti-T in the serum of certain cancer patients may prove valuable in the monitoring of disease progression. (Author abstract) (23 Refs)

91. IMMUNOSUPPRESSION IN PLASMACYTOMA: INDUCTION OF SUPPRESSOR CELLS.

Chen Y, Hwang LT, Heller P

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Clin Exp Immunol; 47(1):191-196 1982

Immunosuppression in BALB/c mice with plasmacytomas (PC) is, at least in part, due to increased suppressor activity of splenic adherent cells. A PC subcellular fraction rich in intracisternal A particles, previously shown to have an immunosuppressive effect in normal BALB/c mice, is now shown to exert this effect through the development of splenic suppressor cells. The splenic suppressor cells induced with this subcellular fraction were found to be radioresistant adherent macrophages that suppressed the immune response of normal splenic cells to sheep erythrocytes through a diffusible factor, but did not influence their polyclonal IgM secretion after LPS stimulation in vitro. These characteristics are identical to those of the naturally occurring suppressor macrophages in mice with PC. Whether the induction of suppressor cells is due to the intracisternal A particles themselves or a factor co-purified with them, remains to be established. (Author abstract) (24 Refs)

92. FUNCTIONAL STUDIES ON B CELLS IN HUMAN BONE MARROW: IN VITRO MITOGEN STIMULATION OF NORMAL AND MALIGNANT B CELLS.

Hammarstrom L, Smith CI, Pettersson D, Mellstedt H, Holm G
Dept. Immunobiology, Wallenberg-laboratory, Karolinska Inst., Lilla Frescati, S-104 05 Stockholm 50, Sweden
Clin Exp Immunol; 43(1):157-164 1981

Using the protein A plaque assay, bone marrow cells from normal donors were shown to secrete spontaneously immunoglobulins mainly of the IgG and IgA class. After mitogenic activation, a marked increase in IgM production was observed with kinetics and cell density requirements similar to that of blood lymphocytes. In Morbus Waldenstrom patients, IgM was the predominant Ig class secreted spontaneously by bone marrow cells. The high in vitro background proliferation of these cells could be abolished by addition of the appropriate anti-idiotypic antiserum. After stimulation with mitogens, differentiation of cells within the malignant clone to immunoglobulin-secreting lymphocytes was evidenced, suggesting a retained responsive capacity of the transformed cells. (Author abstract) (27 Refs)

93. NATURAL KILLER ACTIVITY OF GUT MUCOSAL LYMPHOID CELLS IN MICE.

Tagliabue A, Luini W, Soldateschi D, Boraschi D
Sclavo Res. Center, Via Fiorentina 1, I-53100 Siena, Italy
Eur J Immunol; 11(11):919-922 1981

Intraepithelial lymphoid cells (IEL) obtained from the mucosa of mouse small intestine were tested for natural killer (NK) activity in a 20-hr 51Cr-release assay against YAC-1 and RL male 1 tumor cells. It was found that IEL possess a strong NK activity, higher than spleen cells, whereas lymphocytes from Peyer's patches (PPL) did not show any NK activity. The cytotoxic activity of IEL could be boosted by interferon (IFN-beta) treatment, but no NK activity could be induced in PPL by in vitro IFN-beta treatment. The characteristics of the NK effector cells present in the mouse intestine strictly resemble those of NK cells in the spleen. In fact, intestinal NK activity is not affected by depletion of adherent cells and only partially reduced by anti-Thy-1.2 antibodies plus complement. Moreover, the age dependency of NK cytotoxicity is identical for IEL and spleen. Finally, NK-insensitive target cells are not lysed by IEL. (Author abstract) (17 Refs)

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TUMOR ANTIBODY PRODUCTION/ CHARACTERIZATION/ DETECTION

1. DEVELOPMENT OF A MONOCLONAL ANTIBODY AGAINST A TUMOR-ASSOCIATED ANTIGEN.

Peng WW, Bressler JP, Tiffany-Castiglioni E, De Vellis J
Lab. Nuclear Medicine and Radiation Biology, Univ. California, Los Angeles, CA, 90024
Science; 215(4536):1102-1104 1982

A monoclonal antibody-producing hybrid cell line was obtained by fusing mouse myeloma cells with spleen cells from a mouse immunized with C6 glioma cells. This antibody binds to a specific cell-surface antigen that is present on C6 rat glioma cells, transformed astrocytes and oligodendrocytes, and a human glioma cell line but is absent on a normal glial cell line, fibroblasts, and primary cultures of astrocytes and oligodendrocytes. The antigen also appears on tumor tissue of transformed oligodendrocytes but not on normal brain tissue. (Author abstract) (18 Refs)

2. SCINTIGRAPHY AND DISTRIBUTION OF LABELED ANTIBODIES IN RATS WITH TUMORS.

Sharp JG, Osborne JW, Cheng HF, Coop KL, Zimmerman GR
Radiation Res. Lab., Univ. Iowa, Iowa City, IA, 52242
Eur J Nucl Med; 7(1):28-34 1982

Experiments with in vivo localization of iv injected radiolabeled tumor antibodies (Ab) in Holtzman rats with an x-ray-induced mucoid adenocarcinoma of the intestine are described. Tumor antigen was induced in New Zealand white rabbits using tissue from several animals, and the rabbit serum globulins were separated by electrophoresis and labeled with 131I. Globulins receiving final electrophoretic and diffusion separation were called 'purified'; others were 'unpurified.' The distribution of 131I-labeled unpurified and purified Ab, 131I-labeled non-tumor-specific gamma globulin, and 131I-labeled serum albumin were studied in normal and tumor-bearing rats. Scanning was accomplished by rectilinear camera and gamma camera; tissue distribution of labeled material was determined by scintillation spectrometry of digested tissue samples. Comparison of scans revealed tumors greater than 2.0 g in mice receiving all three radio-labeled agents, but none showed tumors dependably when the tumors were less than 1.0 g. Localization of 131I-labeled Ab was variable, and useful levels of Ab were present in only a few cases. The presence of circulating tumor antigens capable of binding the Ab is responsible for much of the variability. (31 Refs)

3. MONOCLONAL ANTIBODIES TO TWO MOUSE BLADDER CARCINOMA ANTIGENS.

Hellstrom I, Rollins N, Settle S, Chapman P, Chapman WH, Hellstrom KE
Program Tumor Immunology, Fred Hutchinson Cancer Res. Center, Seattle, WA, 98104
Int J Cancer; 29(2):175-180 1982

Carcinomas of the urinary bladder of mice were induced by 3-methyl-cholanthrene or FANFT [(4-5-nitro-2-furyl)-2-thioazolyl formamide]. On transplantation in vivo, tumor lines consisting of well-differentiated transitional-cell carcinomas were established. Some tumors were also explanted in vitro. A rat was immunized with a pool of carcinomas and normal bladder tissue and its spleen cells were hybridized with NS-1 mouse myeloma cells. Supernatants of hybrid cells ('hybridomas') were screened for antibody binding to antigens present in bladder carcinomas but not in normal syngeneic urinary bladder, with cell extracts as targets. Hybridomas that appeared to have the required specificity were cloned, tested further against transitional-cell bladder carcinomas, an anaplastic bladder tumor, rhabdomyosarcomas, a mammary carcinoma, myelomas and lymphomas, and normal adult urinary bladder, kidney, lung, spleen, heart, brain, thymus, and whole embryo. Antibody formed by one hybridoma, 2H5, gave significant binding to membranes from five of seven transitional-cell carcinomas but not to membranes from any other tissues. A second hybridoma, IE6, formed antibody to an antigen present in bladder carcinomas and normal liver and, in smaller amounts, in several other normal and neoplastic tissues. Fluorescence microscopy established that both antigens were present at the cell surface of transitional-cell bladder carcinomas. Immunoprecipitation and SDS-polyacrylamide gel electrophoresis were used to identify the target antigens from 125I-labeled cell membrane proteins. The antibody formed by 2H5 was found to identify a protein with a mol wt in the range of 140 kilodaltons, which was detected in transitional-cell bladder carcinoma and, in small amounts, in normal bladder. The molecular nature of the antigen defined by hybridoma IE6 is not known. (Author abstract) (25 Refs)

4. IMMUNOLOGIC CLASSIFICATION OF LYMPHOCYTIC LEUKEMIAS BASED ON MONOCLONAL ANTIBODY-DEFINED CELL SURFACE ANTIGENS.

Schroff RW, Foon KA, Billing RJ, Fahey JL
Medical Immunology Res. Lab., Dept. Microbiology and Immunology, Univ. California, Los Angeles, CA, 90024
Blood; 59(2):207-215 1982

A panel of monoclonal antibodies reactive with normal lymphocyte subsets was used to classify cases of lymphocytic leukemia on the basis of cell surface antigen expression. The antibodies employed were commercially available and included a common framework HLA-DR antibody, two pan-T antibodies (Leu-1 and OKT-3), and antibodies defining cytotoxic/suppressor (Leu-2 and OKT-8) and helper/inducer (Leu-3 and OKT-4) subpopulations of normal T lymphocytes. Cases of ALL could be subgrouped into non-T non-B, pre-T and T-ALL on the basis of reactivity with HLA-DR, Leu-1, and OKT-3 antibodies. Leukemic cells from patients with T-cell CLL could be divided into Leu-2/OKT-8 reactive and Leu-3/OKT-4 reactive subpopulations, as well as a subgroup in which the majority of cells were unreactive with either of these antibodies. With the exception of one individual, all Sezary cell leukemias expressed a phenotypic pattern similar to that of the Leu-3 subgroup of T-CLL. Malignancies of B-cell lineage (B-CLL, prolymphocytic leukemia, and lymphosarcoma) that were examined were reactive with both the HLA-DR and Leu-1 antibodies. On the contrary, normal B lymphocytes and lymphoid cell lines of B-cell origin did not express surface antigens recognized by the Leu-1 antibody. (Author abstract) (56 Refs)

5. CHARACTERIZATION OF NORMAL AND MALIGNANT HUMAN LYMPHOID CELL POPULATIONS.

Ford RJ
Dept. Pathology, Univ. Texas M.D. Anderson Hosp. and Tumor Inst., Houston, TX
Cancer Bull; 33(6):255-260 1981

Characterization of human lymphoid cell populations with both conventional cell membrane markers and monoclonal antibodies is reviewed. The most reliable human T-cell marker is the sheep red blood cell rosette assay, usually performed with neuraminidase-treated sheep RBC. The cell-surface immunoglobulin receptor is the most reliable human B-cell marker; others include the membrane receptor for Epstein-Barr virus and the mouse RBC membrane receptor. Monocytes and macrophages may be identified and separated by means of the phagocytosis of latex particles; in addition, enzymes such as alpha-naphthylacetate esterase are relatively specific for the monocyte/macrophage system when present in a diffuse cytoplasmic staining pattern. Hybridoma technology has given rise to the use of mouse monoclonal antibodies for identifying various types of human lymphocytes. Panels of monoclonal antibodies with defined specificities will probably make conventional cell markers obsolete in the near future. Conventional immunologic markers for a number of neoplastic lymphoid cells, including T- and B-cell lymphomas and leukemias and histiocytic lymphomas, are discussed. Recent studies concerning the use of monoclonal antibodies for differentiation of lymphoma and lymphocytic leukemia subtypes are described. (38 Refs)

6. ECTOPIC PRODUCTION OF PLACENTA-'SPECIFIC' TISSUE PROTEINS (PP5 AND PP11) BY MALIGNANT BREAST TUMORS.

Inaba N, Renk T, Daume E, Bohn H
(c/o Bohn) Res. Laboratories, Behringwerke AG, Postfach 1140, D-3550 Marburg (Lahn), W. Germany
Arch Gynecol; 231(1):87-90 1981

An enzyme-bridge immunoperoxidase technique was used to demonstrate the production of two placenta-'specific' tissue proteins, PP5 and PP11 in sections of the breast cancers of 16 patients. The specific antisera against human PP5 and PP11 were raised by immunizing rabbits with the purified antigens. An IgG fraction of goat antiserum against rabbit immunoglobulin was used as the second antibody. Peroxidase-rabbit antiperoxidase (PAP) complex was then applied. A slightly modified Mason PAP method was used to demonstrate the tissue antigens. Clear positive staining for PP5 was observed in 10/16 (62.5%) breast cancers, and for PP11 in 7/15 (46.7%). Positive staining was only observed in the cytoplasm. All of the specimens positive for PP11 were also positive for PP5; all six specimens negative for PP5 were also negative for PP11. Positive staining was more frequent in cells found in the periphery of the cancer mass than those in the center. No staining was observed in apparently normal breast tissues and histiocytes in the tissues and/or in the vessels. These determinations in sera might be of use in screening for breast cancer and for monitoring therapy or detecting metastases in patients with established disease. (17 Refs)

TUMOR ANTIBODIES ASSOCIATED WITH VIRUSES

7. NEW DEVELOPMENTS IN THE FIELD OF VIRUSES IN LIVER DISEASE.

Buffet C
Service d'hepatologie et de gastro-enterologie, hopital Bicetre, 78, rue du General-Leclerc, 94270 Kremlin-Bicetre, France
Rev Prat; 31(59):4251-4254 1981

Hepatitis A, the significance of hepatitis B virus (HBV) markers, HBV marker in alcoholics, HBV and carcinogenesis, and non-A, non-B (NANB) hepatitis virus are discussed. HBV antigens and antibodies (antibodies to HBV surface and core antigens and those related to viral replication) are discussed in relation to the diagnosis of hepatitis B. HBV markers are elevated in alcoholic populations (40%) as compared with normal blood donors (10%). In most alcoholics, HBV markers indicative of former, non-developing HBV infection are observed. The role of HBV in cirrhosis is discussed. Integration of HBV DNA in the cellular genome of hepatoma tissue has been demonstrated. Epidemiologically, geographic zones with a high incidence of hepatitis are strictly superimposable over zones with a high incidence of hepatomas. Patients positive for HBV antigens with or without cirrhosis show a higher incidence of liver neoplasms. Although other factors are involved in tumorigenesis in the liver, HBV is directly involved in the development of hepatomas. Identification, transmission, and characteristics of NANB hepatitis virus and resultant infection are described. (13 Refs) (In FRE)

8. CORRELATION BETWEEN VARIANT TRANSLOCATION AND EXPRESSION OF IMMUNOGLOBULIN LIGHT CHAINS IN BURKITT'S LYMPHOMAS AND LEUKEMIAS.

Lenoir G, Preud'homme JL, Bernheim A, Berger R
Programme des Mecanismes de la Cancerogenese, Centre international de Recherche sur le Cancer, 150, cours Albert-Thomas, 69372 Lyon Cedex 2, France
C R Acad Sci [III] (Paris); 293(8):427-429 1981

Expression of immunoglobulins (IG) in Burkitt's lymphomas (19 lines) and leukemias (1 line) are discussed in relation to observed chromosome abnormalities. Of the 19 lymphoma lines, 12 were non-endemic and 7 did not contain the Epstein Barr virus. IG light chains produced varied according to the type of translocation. In 17/18 cases with translocation t(8;14), the light chains of surface and cytoplasmic IG were type kappa (9 cases) or type gamma (8 cases). The cells of patient 18 did not express any detectable light chains. In 3/5 cases of translocation t(2;8), the light chains were type kappa with light chain expression in 1/3; the two other cell lines exhibited a pre-B phenotype. Of six cases with translocation t(8;22), IG with gamma chains were found in 5 and a pre-B phenotype in the sixth. IgM, sometimes associated with IgD, was found in 17/19 cell lines; two cell lines were characterized by monoclonal gamma IgG (translocation t(8;14) in one case and t(8;22) in the other). The results indicated the existence of a relationship bet ween translocations t(2;8) and t(8;22) and light chain expression: kappa in the case of t(2;8) and gamma in the case of t(8;22). (12 Refs) (In FRE)

9. IDENTIFICATION OF EPSTEIN-BARR VIRUS STRAIN DIFFERENCES WITH MONOCLONAL ANTIBODY TO A MEMBRANE GLYCOPROTEIN.

Qualtiere LF, Chase R, Vroman B, Pearson GR
(c/o Pearson) Dept. Cell Biology and Microbiology, Mayo Foundation, Rochester, MN, 55901
Proc Natl Acad Sci USA; 79(2):616-620 1982

Two monoclonal antibodies directed against Epstein-Barr virus (EBV)-induced membrane antigens (MA) were isolated in this study. One of the monoclonal antibodies, designated 2F5.6, was an IgG2 which, as detected by membrane and fixed cell immunofluorescence, reacted with MA-positive lymphoblastoid cell lines that produced transforming EBV but not with the MA-positive P3HR-1 cell line that produced the lytic, non-transforming strain of this virus. This antibody precipitated the Mr 320,000/350,000 glycoprotein from B-95 virus infected cultures and the Mr 300,000 and 220,000/250,000 glycoproteins from Raji cells superinfected with P3HR-1 virus but did not precipitate any of these EBV-specific glycoproteins from the P3HR-1 cell line. In contrast, the second monoclonal antibody, IgM designated B10.3, reacted with all virus-producing cell lines including the P3HR-1 cell line. The identity of the glycoprotein that serves as the target for this antibody is still unknown. Neither antibody had neutralizing activity against the B-95 or P3HR-1 strain of EBV. These results indicated that the 2F5.6 monoclonal antibody was directed against an antigenic determinant on the major membrane glycoprotein which is common to transforming strains of EBV but absent from the lytic P3HR-1 strain whereas the B10.3 monoclonal antibody was directed against a group-specific EBV-induced membrane determinant. (Author abstract) (25 Refs)

10. RESISTANCE TO MOLONEY MURINE SARCOMA VIRUS (M-MUSV) TUMOR INDUCTION IS ASSOCIATED WITH NATURAL ANTIBODY PRODUCTION TO 'ENDOGENOUS' MOLONEY LEUKEMIA VIRUS (M-MULV) IN BALB/MO MICE.

D'Andrea E, De Rossi A, Chieco-Bianchi L
Laboratorio di Oncologia, Istituto di Anatomia Patologica, Via Gabelli 61, 35100, Padova, Italia
Tumori; 67(6):511-520 1981

BALB/Mo mice are characterized by early expression of 'endogenized' M-MuLV and are resistant to M-MuSV tumor induction. Furthermore, compared to normal BALB/c mice, sera from BALB/Mo mice exhibit a significant reactivity which is specific for M-MuLV when tested in a 125I-labeled Staphylococcus protein A binding assay. The possible significance of this reactivity in conferring tumor resistance is explored. (Author abstract) (54 Refs)

11. MALIGNANT LYMPHOMA OF SMALL CLEAVED LYMPHOCYTES OF THE FOLLICULAR MANTLE ZONE.

Palutke M, Eisenberg L, Mirchandani I, Tabaczka P, Husain M
Dept. Pathology, Wayne State Univ. Sch. Medicine, 540 East Canfield Ave., Detroit, MI, 48201
Blood; 59(2):317-322 1982

We describe a highly unusual lymphocytic lymphoma. It appeared to originate in the mantle zones of hyperplastic follicles that had large reactive centers. The tumor cells in the mantle zone were small lymphocytes with cleaved or very irregular nuclei. They had coarse and abundant IgM, kappa surface immunoglobulin markers, and receptors for complement. The tumor involvement was generalized at the time of discovery. The diagnosis of a malignant lymphoma was initially made with difficulty because of the presence of reactive follicular centers as well as a polyclonal hypergammaglobulinemia and large numbers of interfollicular plasma cells and plasmacytoid lymphocytes containing all classes of immunoglobulin. However, 2 yr later, the follicular centers were replaced by tumor nodules composed of lymphocytes identical in appearance and immunologic type to those seen originally. This case illustrates that not all nodular lymphomas are follicular center cell (FCC) neoplasms and that morphological transformation from small round to small cleaved lymphocytes and a corresponding increase in surface immunoglobulins may take place in the follicular mantle zone. The patient had a high titer of antibody to Epstein-Barr virus (EBV) and a poor lymphocyte response to concanavalin A, but neither the tumor cells nor the plasmacytoid lymphocytes contained EBV DNA. (Author abstract) (10 Refs)

12. NATURAL ANTIBODIES TO HUMAN RETROVIRUS HTLV IN A CLUSTER OF JAPANESE PATIENTS WITH ADULT T CELL LEUKEMIA.

Robert-Guroff M, Nakao Y, Notake K, Ito Y, Sliski A, Gallo RC
Dept. Cell Biology, Litton Bionetics, Inc., Kensington, MD, 20895
Science; 215(4535):975-978 1982

Human T cell lymphoma leukemia virus (HTLV) is a human retrovirus (RNA tumor virus) that was originally isolated from a few patients with leukemias or lymphomas involving mature T lymphocytes. Here we report that the serum of Japanese patients with adult T cell leukemia, but not the serum of tested normal donors, contains high titers of antibodies to HTLV. These observations, together with data from Japan showing that adult T cell leukemia is endemic in southwest Japan, suggest that HTLV is involved in a subtype of human T cell malignancy, including Japanese adult T cell leukemia. (Author abstract) (22 Refs)

13. TUMOUR CELL-ANTIBODY INTERACTIONS. II. IN VITRO STUDIES.

Froese G, Berczi I, Israels LG
Manitoba Cancer Res. and Treatment Foundation, Univ. Manitoba, Winnipeg, Manitoba, Canada
Immunology; 45(2):313-323 1982

The interaction of L5178Y thymic lymphoma cells syngeneic to DBA/2 mice and of normal thymocytes with goat IgG antibodies was studied in vitro. Viable tumor and normal cells exerted a rap id, continuous and temperature-dependent destruction of antibody activity. Fractionation studies of culture supernatants from antibody-coated cells revealed that a significant portion of the antibody was completely degraded to amino acids. Tumor cells digested antibody more effectively than did normal lymphocytes. This observed degradation of antibody was most extensive at 37 C, significantly less at room temperature (23 C) and not detectable at 0 C. Undegraded antibody released from antibody-coated cells had also lost its antibody activity to a considerable extent. This was due to the formation of soluble antigen-antibody complexes, which was observed even at 0 C. Cells fixed with 10% formalin bound maximum amounts of antibody were incapable of digesting antibody even at 37 C and did not release immune complexes. These findings are of relevance to cancer immunodiagnosis and immunotherapy. (Author abstract) (40 Refs)

14. ABNORMAL ANTI-EPSTEIN BARR VIRUS ANTIBODIES IN CARRIERS OF THE X-LINKED LYMPHOPROLIFERATIVE SYNDROME AND IN FEMALES AT RISK.

Sakamoto K, Seeley JK, Lindsten T, Sexton J, Yetz J, Ballow M, Purtilo DT
(c/o Purtilo) Dept. Pathology and Lab. Medicine, Univ. Nebraska Medical Center, 42nd and Dewey Ave., Omaha, NE, 68105
J Immunol; 128(2):904-907 1982

The asymptomatic hemizygous female carriers of the x-linked lymphoproliferative syndrome (XLP) have abnormal antibody responses to EBV. This suggests partial expression of the defect that leads to EBV-provoked life-threatening diseases in their affected sons. EBV specific antibodies were measured in 65 serum samples of 12 obligate carrier females and 7 of their daughters (females at risk) during periods ranging from 1 to 5 yr. Abnormal qualitative antiviral capsid antigen (VCA) IgG titers were nearly fourfold higher than normal controls, two carriers had persistent IgM anti-VCA antibody, two-thirds had persistent IgA anti-VCA antibody, and half of the women had titers to early antigen (EA). Five of seven females exhibited a similar persistent pattern. In contrast. none of the unaffected family members nor 23 normal controls expressed IgA or IgM titers to VCA even with high exposure to the virus, and anti-EA was detected in only one control. Therefore, these findings may prove useful for detecting carriers of the syndrome. Abnormal anti-EBV titers similar to the carrier pattern have been reported in patients and other immunosuppressed individuals, and are indicative of active viral infection. (Author abstract) (31 Refs)

15. GENETIC CONTROL OF SENSITIVITY TO MOLONEY LEUKEMIA VIRUS IN MICE: V. ROLE OF H-2-LINKED GENES IN THE CONTROL OF ANTI-FMR CYTOLYTIC T-LYMPHOCYTES.

Duprez V, Debre P, Levy JP
Laboratoire Immunologie et Virologie des Tumeurs, INSERM U 152, Hopital Cochin, Paris 14e, France
Cell Immunol; 65(2):317-324 1981

Three H-2-linked genes, Rmv1, Rmv2, and Rmv3 control the resistance of mice against Moloney virus (MLV)-induced leukemias. It has been shown previously that they function as immune response (Ir) genes regulating the level of antivirus antibodies. In the present experiments, the cell-mediated antitumor response has been studied in a series of inbred strains selected for their resistance or sensitivity to the MLV-induced disease. We failed to detect any relationship between resistance and sensitivity and the ability to produce cytolytic T lymphocytes (CTL) directed against the virus-induced FMR cell surface antigen. Furthermore, the role of each Rmv gene has been studied separately using congenic pairs of mice differing at only one of these loci: we failed to evidence any influence of these genes in the cell-mediated antitumor reactions as measured by the ability to lyse syngeneic FMR(+) target cells. Nevertheless a gene mapping in the D region of the MHC but probably different from RMv3 controls the response of a subset of anti-FMR CTL restricted by the H-2Kk antigens, with higher response in H-2Dd animals than in H-2Db animals. This observation confirms the existence of H-2D region associated Ir genes regulating the CTL-mediated antitumor immune responses by choosing the subset of responder CTL, and suggests that a fourth H-2-linked gene plays some role in the genetic control of the anti-FMR immune response. (Author abstract) (15 Refs)

16. ENDOGENOUS MURINE LEUKEMIA VIRUS-ENCODED PROTEINS IN RADIATION LEUKEMIAS OF BALB/C MICE.

Tress E, Pierotti M, DeLeo AB, O'Donnell PV, Fleissner E
(c/o Fleissner), Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Virology; 117(1):207-218 1982

To explore the role of endogenous retroviruses in radiation-induced leukemogenesis in the mouse, we have examined virus-encoded proteins in nine BALB/c leukemias by pulse-chase labeling procedures and serological typing with monospecific and monoclonal antibodies. The major gag precursor protein, Pr65gag, was observed in all cases, but only three leukemias expressed detectable amounts of the glycosylated gag species, gP95gag, or its precursor, Pr75gag. No evidence was found for synthesis of gag-host fusion proteins. None of the leukemias released infectious xenotropic or dualtropic virus, but all nine expressed at least one env protein with xenotropic properties. In two instances a monoclonal antibody, 35/56, which is specific for the MuLV GIX antigen, displayed a distinctive reactivity with this class of env protein, although this antibody is unreactive with replicating xenotropic viruses. An ecotropic/xenotropic recombinant env protein with the same 35/56 phenotype was observed in a leukemia induced by a strongly leukemogenic virus isolated from a BALB/c radiation leukemia. (Author abstract) (40 Refs)

17. UNUSUAL INTRACYTOPLASMIC IMMUNOGLOBULIN INCLUSIONS IN CHRONIC LYMPHOCYTIC LEUKAEMIA.

Guglielmi P, Preud'Homme JL, Gourdin MF, Reyes F, Daniel MT
INSERM U 108, Hopital Saint Louis, 75475 Paris Cedex 10, France
Br J Haematol; 50(1):123-134 1982

Unusual intracytoplasmic immunoglobulin inclusions were found by immunofluorescence in three patients with chronic lymphocytic leukemia. The inclusions contained the same immunoglobulin chains as those detected on the plasma membrane, except for delta chains which were expressed on the cell surface and not in the cytoplasmic inclusions. The cytoplasmic staining persisted throughout culture for 8 or more days. An initial study of patient number one's cells showed that the inclusions contained only mu chains, and kappa chains gradually became apparent after in vitro culture. In a second study, the fresh lymphocytes contained both mu and kappa chains. Initially, biosynthetic experiments showed production of mu chains which polymerized in the cytoplasm and were not secreted. Subsequently there was synthesis of heavy and light chains which assembled into monomeric subunits that were retained and secretion of free light chains. The apparent mol wt of these immunoglobulin chains was larger than that of their secretory counterparts. Immunoelectronmicroscopy revealed cytoplasmic mu chains in strands of endoplasmic reticulum. In the two other patients, immunofluorescence displayed unusual staining patterns of bright networks in perinuclear areas. (Author abstract) (31 Refs)

18. EFFECT OF BENZO[A]PYRENE ON FRIEND VIRUS LEUKEMOGENESIS, CFU-S VIABILITY, AND INDUCTION OF HUMORAL IMMUNITY.

Raikow RB, OKunewick JP, Buffo MJ, Jones DL
Cancer Res. Lab., Allegheny-Singer Res. Corp., Allegheny General Hosp., Pittsburgh, PA, 15212
Experientia; 38(1):126-127 1982

The compound benzo[a]pyrene (BP) potentiated the induction of leukemia by low doses of Friend virus in SJL/J mice if injected 2 days before the virus. BP also reduced the viability of hematopoietic stem cells (CFU-S) within this time interval but had little effect on the induction of humoral immunity (the PFC response). (Author abstract) (18 Refs)

19. CORRELATION BETWEEN MIXED LYMPHOCYTE CULTURES AND ANTI-EPSTEIN BARR VIRUS (EBV) ANTIBODIES IN HODGKIN'S DISEASE AND NON HODGKIN LYMPHOMA PATIENTS.

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Biomedicine [Express]; 35(5):153-156 1981

Cellular and humoral immunity was examined in Hodgkin's disease and non Hodgkin lymphoma (33) patients and compared with a normal group. Mixed lymphocyte cultures (MLC) were used as a parameter for cell mediated immunity and anti-Epstein Barr virus (EBV) antibodies for specific humoral immunity. High stimulation indices coincided with low anti-VCA and anti-EBNA titers in the control group (r =-0.343). This negative correlation was not found in non Hodgkin lymphomas and was substantially lower (r =-0.142) in Hodgkin's disease. The alterations in immunoregulatory mechanisms in these patients are discussed. (Author abstract) (29 Refs)

ANTITUMOR ACTIVITY AND IMMUNOTHERAPY

20. NORMAL AND MALIGNANT HUMAN MYELOCYTIC AND MONOCYTIC CELLS IDENTIFIED BY MONOCLONAL ANTIBODIES.

Bernstein ID, Andrews RG, Cohen SF, McMaster BE
Pediatric Oncology Program, Fred Hutchinson Cancer Res. Center, Seattle, WA, 98104
J Immunol; 128(2):876-881 1982

Two cytotoxic IgM monoclonal antibodies reactive with human cells of myeloid origin are described. Each antibody was tested for reactivity with normal and malignant cells of myeloid origin by using immunofluorescent and cytotoxic assays. Antibody 5F1 defines a determinant expressed by peripheral blood monocytes and platelets. Antibody 1G10 detects a determinant expressed in high concentration on granulocytes and in low concentration on a subset of monocytes. Neither antibody reacts with peripheral blood lymphocytes, erythrocytes, or thymocytes. In bone marrow, 5F1 stains monocytic and nucleated erythrocytic cells, whereas 1G10 stains cells of the granulocytic lineage. Each antibody also reacts with subsets of acute nonlymphocytic leukemia cells. These reagents should be useful in delineating stages of normal and malignant myeloid differentiation. (Author abstract) (37 Refs)

21. DEFINITION OF A THY-1 DETERMINANT ON HUMAN NEUROBLASTOMA, GLIOMA, SARCOMA, AND TERATOMA CELLS WITH A MONOCLONAL ANTIBODY.

Seeger RC, Danon YL, Rayner SA, Hoover F
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J Immunol; 128(2):983-989 1982

Neuroblastoma, glioma, rhabdomyosarcoma, leiomyosarcoma, and teratoma cells were shown to express an antigenic determinant of human Thy-1 with monoclonal antibody 390 (ab 390). Specificity of ab 390 for a determinant on Thy-1 was shown in three ways. (1) The distribution of antigenic determinant 390 (ag 390) among normal cells and tissues was that of human Thy-1. Quantitative absorption of ab 390 with adult tissues demonstrated a large quantity of ag 390 associated with brain, at least 90-fold less associated with kidney, and 150 to 10,000-fold less associated with lung, thymus, liver, adrenal, colon, and muscle. Ab 390 reacted strongly with cultured fibroblasts and also with 12% of thymocytes; it did not react with blood monocytes, lymphocytes, erythrocytes, or with bone marrow cells. (2) A molecule was isolated from deoxycholate solubilized human brain membranes by ab 390 affinity chromatography with Mr = 24,000. (3) Human brain Thy-1 that was purified by lentil lectin affinity chromatography specifically inhibited binding of ab 390 to LA-N-1 human neuroblastoma cells. In studies of 29 cultured tumor cell lines, ab 390 reacted strongly with gliomas and moderately with neuroblastomas, a rhabdomyosarcoma, a leiomyosarcoma, and teratomas. Its reactivity with medulloblastoma, melanoma, and carcinoma cell lines was weak or insignificant. A molecule with Mr = 26,000, which is the mw of fibroblast associated Thy-1, was purified from membranes of a neuroblastoma and a glioma cell line. Quantitative absorption of ab 390 with 50 noncultured tumors demonstrated that neuroblastomas, gliomas, and soft tissue sarcomas can express more ag 390 than all adult tissues except brain. Significant heterogeneity in the quantity of ag 390 associated with individual tumors within these positive classes was observed. These data suggest a variety of human tumor cells express Thy-1 on their surfaces. This expression appears to be appropriate for neuroblastoma, glioma, rhabdomyosarcoma, and leiomyosarcoma cells because normal cells of these same lineages also can express Thy-1. (Author abstract) (33 Refs)

22. MONOCLONAL ANTIBODIES TO THE HUMAN MAMMARY GLAND. II. DISTRIBUTION OF DETERMINANTS IN BREAST CARCINOMAS.

Foster CS, Dinsdale EA, Edwards PA, Neville AM
Ludwig Inst. Cancer Res., Royal Marsden Hosp., Sutton, Surrey SM2 5PX, England
Virchows Arch [Pathol Anat]; 394(3):295-305 1982

A range of primary and metastatic human breast carcinomas has been examined with respect to the staining by four monoclonal antibodies which were raised to the human milk fat globule membrane. Within the normal breast the luminal epithelial cells expressing the antigens detected by the monoclonal antibodies were heterogeneous in their distribution. The heterogeneity was not only confined to single cells, but also to regions within the breast. The breast carcinomas also expressed the antigens in a variable manner. Morphological differentiation and functional differentiation, defined by the monoclonal antibodies, were not invariably coincident. Lymph node metastases gave similar results to the primary carcinomas. The monoclonal antibodies have revealed a heterogeneity, with respect to surface antigenic expression, within the normal and neoplastic breast epithelium. This cellular heterogeneity of breast carcinomas, may have significant prognostic and therapeutic implications in the management of primary breast cancer. (Author abstract) (17 Refs)

23. ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY OF LEUKAEMIC BLAST CELLS AND NEUTROPHILS FROM PATIENTS WITH ACUTE MYELOGENOUS LEUKAEMIA.

Dallegri F, Holm G, Gahrton G
ISMI-Clinica Medica R, Universita degli Studi, Viale Benedetto XV n. 6, I-16132 Genova, Italy
Clin Exp Immunol; 47(2):414-418 1982

The antibody-dependent cellular cytotoxicity against ox erythrocytes by blast cells and neutrophils from six patients with acute myelogenous leukemia and one patient with blast crisis of chronic myelogenous leukemia was studied. Leukemic myeloblastic and monocytic cells behaved like potent killer cells toward ox erythrocytes and their activity was comparable with that of neutrophils from leukemic and normal subjects. The target cell destruction was positively related to the effector cell:target cell ratio and was clearly antibody-dependent since the cytotoxic effect did not involve antibody-unsensitized erythrocytes. We suggest that this experimental system, which involves the use of ox erythrocytes sensitized by purified rabbit anti-ox IgG, provides a new and sensitive method for studying antibody-dependent cellular cytotoxicity by myeloid cells. (Author abstract) (11 Refs)

24. HUMAN MONOCLONAL IGM WITH AUTOANTIBODY ACTIVITY AGAINST INTERMEDIATE FILAMENTS.

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Proc Natl Acad Sci USA; 79(2):446-450 1982

Monoclonal IgMs from two patients with Waldenstrom macroglobulinemia were found to react with intermediate filaments. This was shown by (a) immunostaining of various tissues and cultured cells and (b) immunological characterization of the reactive antigen after blotting of polypeptides separated from total cell extracts by gel electrophoresis or purified intermediate filaments on nitrocellulose sheets. One monoclonal IgM had an activity directed only against vimentin, whereas the other reacted with four different classes of intermediate filaments-vimentin, desmin, glial fibrillary protein, and keratins. All of the reactivity of the latter IgM was absorbed by purified vimentin, suggesting that different classes of proteins of intermediate filaments share common antigenic determinant(s). The significance of such autoantibody activity of human monoclonal IgM is discussed in the light of the startling frequency of IgM anti-intermediate filaments antibodies in various diseases. (Author abstract) (32 Refs)

25. A COMPARATIVE STUDY OF THE USE OF MONOCLONAL ANTIBODIES USING THREE DIFFERENT IMMUNOHISTOCHEMICAL METHODS: AN EVALUATION OF MONOCLONAL AND POLYCLONAL ANTIBODIES AGAINST HUMAN PROSTATIC ACID PHOSPHATASE.

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J Histochem Cytochem; 30(3):253-260 1982

The use of immunohistochemical methods has been advocated for the detection and localization of prostatic acid phosphatase in paraffin sections of human prostate. This article explores the possible advantages of utilizing monoclonal antibodies in this method. Monoclonal antibodies, specific for human prostatic acid phosphatase, were integrated into three different immunohistochemical procedures . In the first method, a three-layer peroxidase-antiperoxidase (PAP) system was employed; the monoclonal antibody was followed by rabbit bridge antibody directed against mouse immunoglobulin and mouse PAP complex. The second method was a three-layer system utilizing biotin-labeled horse anti-mouse antibody as 'bridge' antiserum between the primary monoclonal antibody and an avidin-biotin-horseradish peroxidase complex. The third method was a four-layer system; the monoclonal antibody was followed by rabbit anti-mouse serum, swine anti-rabbit immunoglobulin as the bridge antibody and rabbit PAP complex. It was found that some, but not all, monoclonal antibodies can be used for the detection of prostatic acid phosphatase in paraffin sections. The four-layer PAP method was found to be the most sensitive method of the three systems tested; however, the avidin-biotin method required the least amount of time. No significant difference in the quality of staining was observed between monoclonal antibodies and carefully absorbed conventional antiserum. (Author abstract) (12 Refs)

26. ATYPICAL T LYMPHOPROLIFERATIVE DISORDER DEMONSTRATING IN VITRO SUPPRESSOR AND HELPER CHARACTERISTICS.

Proctor SJ, McGregor AM, Clark J, McLachlan S, Dickinson A

Dept. Hematology, Royal Victoria Infirmary, Newcastle upon Tyne, England

Br J Haematol; 50(2):231-240 1982

A patient initially diagnosed on surface marker status as having T cell chronic lymphatic leukemia (T-CLL) was found to have arthropathy and recurrent pulmonary infarction associated with a high anti-DNA antibody titer. The T cells from this patient, on assessment in an in vitro pokeweed mitogen driven B cell system, demonstrated suppressor and helper characteristics but lacked antibody dependent cellular cytotoxicity (ADCC) activity and natural killer (NK) activity. Using peripheral blood mononuclear cells (PBM) from patients with Hashimoto's thyroiditis and normals, it was shown that the patient's T cells suppressed both IgG and thyroid autoantibody production. Irradiation of the patient's PBM inhibited the suppressor effect and a residual helper effect remained. The patient was treated with systemic steroids for exacerbations of arthropathy which caused a fall in lymphocyte count. After 36 mo the DNA binding activity spontaneously improved and the lymphocytosis disappeared. It is indicated that T-cell proliferations demonstrating functional activity must be assessed within the context of any underlying non-hematological clinical and laboratory findings. (Author abstract) (19 Refs)

27. TUMOR BEARER T CELLS SUPPRESS BCG-POTENTIATED ANTITUMOR RESPONSES. I. REQUIREMENTS FOR THEIR EFFECT.

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Cell Immunol; 66(1):121-138 1982

Mice bearing established syngeneic tumors fail to reject them when immunized according to protocols based on optimal conditions for BCG potentiation of specific delayed-type hypersensitivity (DTH) and antitumor immunity. Serum factors from mice bearing either the poorly immunogenic mastocytoma, P815 (MA), or the more antigenic sarcoma, Meth A, have been shown to depress both DTH and antitumor immunity. This report demonstrates that lymphoid cells adoptively transferred from these tumor-bearing hosts also can suppress the efferent and afferent phases of DTH to tumor-specific antigens in both BCG-primed and unprimed syngeneic hosts. Suppressor cells (SC) were detected in spleen, thymus, and lymph nodes draining the tumor site, but not in distant superficial lymph nodes. Maximal suppressor activity appeared 6 days after tumor implantation and wanted by 18 days. Suppression of the afferent phase of both the BCG-primed and unprimed responses was antigen specific; suppression of the efferent phase of the BCG-primed response was also specific but SC could partially suppress the unprimed responses to sheep red blood cells (SRBC). Amputation of 6-day-old tumors resulted in the disappearance of splenic SC within 2 days but did not affect SC in draining lymph nodes. SC suppressed DTH in a dose-dependent manner but even the highest doses tested did not totally eliminate the response. Depression of the peak DTH reaction was not accompanied by significant abrogation of antitumor activity. If, however, SC were transferred during the ongoing antitumor response, immunity was partially suppressed. Efferent-phase SC were sensitive to treatment with anti-Thy 1 sera and complement but were unaffected by B-cell depletion. (Author abstract) (29 Refs)

28. EFFECT OF TOXIN-ANTIBODY CONJUGATES ON TUMOR CELLS.

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Cell Immunol; 66(1):24-28 1982

An attempt was made to use a specific antibody to deliver a toxin (ricin, a highly toxic plant lectin) to tumor cells. Conjugates (anti-muA) of rabbit anti-mu and A chains of ricin were prepared. Murine B lymphocytes bearing IgM were exposed to anti-muA. A binding assay showed that the conjugate retained specificity for IgM. Toxicity was assayed by stimulating BALB/c mouse spleen cells with lipopolysaccharide and then exposing the cells to anti-muA. Anti-muA at concentrations of 5-10 ug/ml inhibited protein synthesis in the cells by 80%. Protein synthesis was not inhibited by treatment with conjugates of normal rabbit immunoglobulin and A chain or with unconjugated antibody. Since ricin functions by inhibition of protein synthesis, results indicate that anti-muA retained antigen-specific toxicity. Spleen cells from mice bearing BCL1 tumors were exposed in vitro to conjugates of anti-idiotype antibodies and A chains (anti-iA). Anti-iA inhibited protein synthesis in the spleen cells by 70%. Since spleens from the tumor-bearing mice consisted of approx 70% BCL1 cells, results indicate that anti-iA is capable of specific destruction of a particular population of tumor cells. A strategy of nonimmunologic reduction of pathologic cell population followed by elimination of surviving cells with anti-idiotypic-ricin conjugates is suggested for treatment of leukemia. (4 Refs)

29. IMMUNOLOGICAL MONITORING OF PATIENTS AFFECTED BY ANAPLASTIC GLIOMA CONCERNING THE EFFECTS OF SURGERY, RADIO-, AND CHEMOTHERAPY: A PRELIMINARY REPORT.

Servadei F, Parente R, Spagnolli F, Gaist G, Padovani R, Bucci M, Steiner L

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Acta Neurochir (Wien); 60(1/2):71-80 1982

The authors studied 24 patients affected by anaplastic gliomas as regards immunology. In all of them the authors evaluated the lymphocyte subpopulation (B and T), firstly by simple lymphocyte count, secondly by studying the rosettes E-total and EAC, thirdly by stimulating the lymphocytes with mitogens phytohemagglutinin-P (PHA), concanavalin A (Con A), and pokeweed mitogen (PWM), and lastly by counting the release of Cr51 in Chang liver cells culture in order to obtain antibody dependent cellular cytotoxicity (ADCC). The parameters were also evaluated after surgery and during conventional radio-chemotherapy with BCNU. Whereas the so-called B-pool seems to be unaffected, the preliminary results show that the T-pool (identified by the E-t rosettes and by responses to PHA, PWM, and ConA) is depressed to a statistically significant degree, if compared with a control group. This depression seems to be related to the tumoral mass, and it is not increased by radio-chemotherapy. In addition, ADCC also seems to be depressed in our glioma patients in comparison with a control group and with a group of bladder cancer patients. (Author abstract) (36 Refs)

30. EVALUATION OF ANTIBODY-DEPENDENT CELL CYTOTOXICITY (ADCC) AND SPONTANEOUS LYMPHOCYTE-MEDIATED CYTOTOXICITY (SLMC) IN PATIENTS SUFFERING FROM MALIGNANT DISEASE.

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G Clin Med; 62(9):609-623 1981

The immune system and the evolution of malignant neoplasia were studied in 36 patients with cancer. Lymphocytes B, T, and EA rosette formation were determined in normal controls (NC: 20-70 yr old patients) with different diseases (DD), with localized cancer (LC: pulmonary, mammary, digestive tract, melanomas etc), with metastasizing cancer (MC: mammary cancer with bone and brain metastases, colon cancer with hepatic metastases and bladder cancer with bone and lymph node metastases), patients receiving polychemotherapy (PCT) with 5-fluorouracil and dacarbazine, patients receiving cyclophosphamide (CYP), and patients receiving radiotherapy (RT). Antibody-dependent cell cytotoxicity (ADCC) and spontaneous lymphocyte-mediated cytotoxicity (SLMC) were present in all NC with values slightly lower in older persons and women. The values for lymphocytes B, T, and EA rosette for NC were on the av 10%, 55%, and 8%, respectively, for DD the values were 8%, 53%, and 7% respectively, for not treated LC the values were 7%, 47%, and 7%, respectively, for not treated MC were 8%, 41%, and 6% respectively, for PCT were 7%, 38%, and 6%, respectively, for treated with CYP the values were 4%, 22%, and 3%,respectively, and for treated with RT the values 2%, 7%, and 2%, respectively. Natural Killer cell activity was significantly decreased in MC patients. Differences of lytic response in vitro were not related to T/B lymphocyte ratio in 90% of the cases. (5 Refs) (In ITA)

31. TUMOUR CELL-ANTIBODY INTERACTIONS. I. IN VIVO EXPERIMENTS.

Froese G, Berczi I, Israels LG

Manitoba Cancer Res. and Treatment Foundation, Univ. Manitoba, Winnipeg, Manitoba, Canada

Immunology; 45(2):303-312 1982

Goats were immunized with membrane fractions of the L5178Y tumor syngeneic to DBA/2 mice. IgG fractions of this antiserum were made tumor specific by repeated in vitro and in vivo absorptions with normal cells and concentrated by adsorption to and elution from tumor cells. In vivo studies indicated that the accumulation of 125I-labelled antibody in tumor tissue could not be improved by extensive purification and concentration. The observed clearance rates of radioactivity from tumors and whole animals showed that the metabolism of antibodies was significantly accelerated in the presence of target cells. It is suggested that a rapid neutralization and degradation of antibody by the target tissue prevents its accumulation in tumor nodules. (Author abstract) (22 Refs)

IMMUNOGLOBULIN STRUCTURE AND SYNTHESIS

32. DNA BETWEEN VARIABLE AND JOINING GENE SEGMENTS OF IMMUNOGLOBULIN KAPPA LIGHT CHAIN IS FREQUENTLY RETAINED IN CELLS THAT REARRANGE THE KAPPA LOCUS.

Van Ness BG, Coleclough C, Perry RP, Weigert M
Inst. Cancer Res., Fox Chase Cancer Center, Philadelphia, PA, 19111
Proc Natl Acad Sci USA; 79(2):262-266 1982

A systematic analysis of the fate of the DNA between kappa chain variable (Vkappa) and joining (Jkappa) genes in cells that have rearranged kappa loci was carried out. The DNA from a variety of kappa-producing plasmacytomas, lambda-producing hybridomas, and kappa-expressing lymphocytes was digested, fractionated by size, and analyzed with two probes containing sequences 5' or Jkappa. In 13 of 28 plasmacytomas examined the rearrangement of Vkappa and Jkappa appears to be accompanied by loss of DNA upst ream of Jkappa. However, in the rest of the plasmacytomas one or more upstream sequences are retained in a new context. In 9 of 12 lambda-producing hybridomas (which frequently rearrange both kappa loci) one or more upstream segments were detected. These unique fragments were probably generated by a recombination event near or at the Jkappa region. The extent to which the region between V and J is maintained in kappa-expressing lymphocytes was also measured. Most (76%) of the region upstream of Jkappa is retained in the population, even though 68% of the kappa loci are rearranged. In order to explain how these upstream elements occur in some, but not all, cell lines, and the significant occurrence in the lymphocyte population, we propose a model in which a step in V-J joining involves mitotic recombination by unequal sister chromatid exchange. (Author abstract) (20 Refs)

33. IMMUNE RESPONSE TO PHOSPHORYLCHOLINE. IX. CHARACTERIZATION OF HYBRIDOMA ANTI-TEPC15 ANTIBODIES.

Wittner MK, Bach MA, Kohler H
Dept. Pathology, La Rabida-Univ. Chicago, Chicago, IL, 60649
J Immunol; 128(2):595-599 1982

Hybridoma antibodies against the PC-binding T15 BALB/c myeloma protein were raised by cell fusion with anti-T15 A/He immune cells. The idiotype specificity of these monoclonal anti-T15 antibodies was determined with a panel of different myeloma and hybridoma immunoglobulins. Two types of anti-T15 antibodies are seen. One reacts with a number of different IgA myeloma proteins and with serum IgA of certain strains of mice; this reactivity most likely is due to allotypy. The other group consists of anti-T15 antibodies that are specific for the T15 idiotype and are therefore termed anti-idiotypic. The bindings of the anti-idiotype antibodies to T15 were specifically inhibited by T15 F(ab')2 but not by other PC-binding myeloma proteins of different idiotypes. The relationship of the idiotype-specific anti-T15 antibodies to the PC-binding site of the T15 idiotype was analyzed by hapten inhibition of anti-idiotypic binding and by inhibition of BALB/c anti-PC splenic hemolytic plaque formation. Anti-T15 antibodies, for which the T15 binding is inhibited by PC or PC-BSA, also specifically inhibit anti-PC plaque formation. These antibodies are labeled site and near-site anti-idiotypic antibodies. Site and near-site-specific anti-idiotypic antibodies recognize different idiotopes on the T15 molecules. The possible differential biologic activities of these anti-idiotopes in idiotype network regulation is considered. (Author abstract) (30 Refs)

34. THE REQUIREMENT FOR ESTERASE ACTIVATION IN T CELL REPLACING FACTOR (TRF)-INDUCED IGG PRODUCTION IN A HUMAN B BLASTOID CELL LINE.

Miki Y, Kishi H, Muraguchi A, Kishimoto S, Yamamura Y, Kishimoto T

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J Immunol; 128(2):675-678 1982

Involvement of stimulus-activatable serine esterase in the process of TRF-induced IgG production in a human B blastoid cell line (CESS) was demonstrated. Addition of DFP or PMSF (1 x 10(-3) M to 1 x 10(-5) M) showed a dose-dependent inhibitory effect on TRF-induced IgG induction in CESS cells. Other organophosphorous inhibitors, such as p-NPEPP and PEPP, were also effective, but a non-phosphorylating analogue of DFP, DMP, was not inhibitory. Simultaneous addition of DFP with TRF showed the inhibitory effect, and the inhibition was irreversible. However, pretreatment on the cells with DFP did not abrogate TRF-induced IgG production. In synchronized cells, signals provided by TRF could be transduced only when cells were in the G1-phase, and DFP showed an inhibitory effect only when it was added to cells in the G1-phase with TRF. One amino acid derivative (AAME) partially inhibited TRF-induced IgG production. (Author abstract) (23 Refs)

35. IMMUNOGLOBULIN PRODUCTION IN HUMAN MIXED LYMPHOCYTE CULTURES: IMPLICATIONS FOR CO-CULTURES OF CELLS FROM PATIENTS AND HEALTHY DONORS.

Rumke HC, Terpstra FG, Huis B, Out TA, Zeijlemaker WP

Central Lab., The Netherlands Red Cross Blood Transfusion Service, Amsterdam, The Netherlands

J Immunol; 128(2):696-701 1982

When human peripheral blood lymphocytes (PBL) are cultured in the presence of irradiated allogeneic lymphocytes, the resulting mixed lymphocyte reaction (MLR) leads to the secretion into the supernatant of substantial amounts of IgM and IgG, derived from nonirradiated responder B lymphocytes. Our data indicate that stimulation to Ig production by responder B cells may result from different types of interactions. First, B cells and monocytes among the irradiated stimulator cells activate T cells in the responder population, which in turn trigger responder B cells to produce Ig; second, 'responder' B cells activate irradiated 'stimulator' T cells, leading to a 'helper' signal, back to the responder B cells and leading to Ig production. The latter system is radiosensitive, because allogeneic T cells, irradiated at a dose of 4,000 rad or more, failed to induce Ig production by responder B cells. In some combinations of human allogeneic lymphocytes, the co-culture of the cells leads to inhibition of Ig production, both in the presence and in the absence of PWM. Thus, co-culture of allogeneic cells may cause 'positive' as well as 'negative' allogeneic effects. The implications of these findings for the interpretation of co-cultures that are aimed at establishing defects in lymphocytes from patients with, for example, immunodeficiencies, who fail to produce Ig in the presence of PWM are discussed. (Author abstract) (21 Refs)

36. MEMBRANE-BOUND AND SECRETED IGA CONTAIN STRUCTURALLY DIFFERENT ALPHA-CHAINS.

Sitia R, Kikutani H, Rubartelli A, Bushkin Y, Stavnezer J, Hammerling U
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J Immunol; 128(2):712-716 1982

Three different forms of alpha-chains are synthesized by BFO.3 and 615.2, two cloned cell lines derived from the murine B lymphoma I.29. The three forms of alpha-chains differ in size, pI, cellular location, and rate of turnover. They were identified by means of lactoperoxidase-catalyzed radioiodination, internal 14C or 35S labeling, and immunofluorescence techniques as membrane-bound(alpham), secreted (alphas), and intracellular (alphaic) proteins. Comparison of immunoglobulin products of the two lymphoma lines with those of a hybridoma cell line, Id 150, which secretes IgA of the I.29 idiotype but lacks membrane IgA, confirmed the assignments of alpham, alphas, and alphaic. Results of biosynthetic labeling of BFO/3, 615.2, and Id 150 in the presence and absence of tunicamycin suggest that the difference in mol wt and charge observed between alpham and alphas can be attributed to differences in primary amino acid structure rather than different degrees of glycosylation. (Author abstract) (28 Refs)

37. CHARACTERIZATION OF SUPPRESSOR CELLS REGULATING IN VITRO EXPRESSION OF IGG2A AND IGG2B ANTIBODY RESPONSES.

Lowy I, Joskowicz M, Theze J
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J Immunol; 128(2):768-773 1982

In vitro cooperative responses between hapten-primed anti-Thy-1.2 plus C-treated spleen cells and carrier-primed T cells have different isotypic patterns depending on the source of the T helper cells. T helper cells from primed lymph node induce IgG1, IgG2a, and IgG2b PFC responses, whereas T helper cells from primed spleen induce only an IgG1 type of response. The addition of activated spleen cells to the lymph node cells suppresses their ability to generate IgG2a and IgG2b PFC responses. The suppressor cells involved have been characterized. Functionally, they appear as nonantigen specific and isotype specific, because they never reduce the IgG1 response. They are Lyt-2.2 positive, Lyt-1 negative, and radiosensitive. Their relative resistance to anti-Thy-1.2 plus C treatment indicates that they express low amounts of this antigen or that they are heterogeneous concerning the expression of Thy-1.2. (Author abstract) (21 Refs)

38. AUTOIMMUNE HAEMOLYTIC ANAEMIA WITH MONOCLONAL IGM (KAPPA) ANTI-P COLD AUTOHAEMOLYSINS.

von dem Borne AE, Mol JJ, Joostra-Maas N, Pegels JG, Langenhuijsen MM, Engelfriet CP
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Br J Haematol; 50(2):345-350 1982

A patient is described with immunoblastic non-Hodgkin's lymphoma and autoimmune hemolytic anemia of the cold autoantibody type. The autoantibodies were monoclonal IgM-kappa cold hemagglutinins/hemolysins with blood-group specificity, anti-P. Red-cell autoantibodies directed against blood-group-P antigen have until now only been detected, as polyclonal IgG antibodies, in paroxysmal nocturnal hemoglobinuria. (Author abstract) (19 Refs)

39. CHARACTERIZATION AND FUNCTIONAL PROPERTIES OF TUMOR CELL LINES IN ACCESSORY CELL REPLACEMENT ASSAYS.

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J Immunol; 128(2):852-859 1982

This study reports the initial phenotypic and functional characterization of a series of cloned, murine, myelomonocytic tumors and their parent cell line WEHI-3, and a group of murine B lymphoma tumors. The tumor cell lines of the myelomonocytic lineage demonstrated the ability to reconstitute a macrophage-depleted, primary in vitro anti-SRBC PFC response, but only marginally enhanced an accessory cell-depleted, ova-primed, lymphocyte proliferation in vitro response. The B lymphoma tumors displayed exactly the reverse functional profile, being highly efficient in reconstitution of the proliferation response, but not supporting the SRBC PFC response. Detailed analysis of the cell surface phenotype of the various B lymphoma tumors used in this study show they display cell surface markers characteristic of normal B lymphocytes but are heterogeneous in their various stages of differential arrest. Future work will concentrate on the orchestration of Ia-mediated and soluble factor-mediated (IL 1) modalities of antigen-triggering of lymphocytes by these B lymphoma and myelomonocytic tumor cell lines. (Author abstract) (46 Refs)

40. STUDIES OF MOUSE IMMUNOGLOBULIN ALLOTYPES BY REVERSE PLAQUE ASSAY: DETECTION OF SPLEEN CELLS SECRETING IMMUNOGLOBULINS WITH SPECIFIC ALLOTYPE IN C57BL/6J MICE.

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(c/o Ansari) Toxicology Center, Northrop Services, Inc., Research Triangle Park, NC, 27709
Cell Immunol; 66(1):164-170 1982

A reverse hemolytic plaque assay for the detection and enumeration of mouse spleen cells secreting immunoglobulins bearing a particular allotypic specificity is described. Sheep red blood cells (SRBC) coated with protein A or anti-mouse gamma globulin antibody were employed as indicator cells and an anti-allotype antibody was used as developer. A comparison of the efficiency of protein A, goat anti-mouse or rabbit anti-mouse gamma globulin antibody-coated SRBC as indicator cells in the plaque assay indicated that the rabbit anti-mouse gamma globulin-coated SRBC gave the best results in terms of the number and morphology of the plaques. The number of indicator cells in the assay mixture also significant ly affected the quality of the plaques formed. When the mouse spleen cells were assayed with the indicator cells and an anti-allotypic antibody as developer in presence of complement in a liquid medium, only those cells secreting the immunoglobulin of the given allotypic specificity formed hemolytic plaques. (Author abstract) (15 Refs)

41. SOMATIC CELL GENETICS OF IMMUNOGLOBULIN PRODUCTION.

Scharff MD
Dept. Cell Biology, Albert Einstein Coll. Medicine, Bronx, NY, 10461
Cell Immunol; 66(1):29-33 1982

Tissue culture lines of mouse myeloma cells have been used to study the somatic cell genetics of immunoglobulin production. Assays have been developed to identify and quantify mutants that have undergone changes in either the synthesis or structure of the immunoglobulin molecule. All of the classical types of mutants have been identified. What is unusual is that these mutants arise at a very high frequency. This genetic instability seems to be restricted to immunoglobulin genes. The fusion of mutant and wild-type cells allows the study of interaction of genes and gene products. (Author abstract) (18 Refs)

42. THE PRESENCE OF MONOCLONAL CYTOPLASMIC IMMUNOGLOBULINS IN LEUKEMIC B CELLS FROM PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA.

Han T, Ozer H, Bloom M, Sagawa K, Minowada J
Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
Blood; 59(2):435-438 1982

It has generally been assumed that CLL B cells do not contain cytoplasmic immunoglobulin (CyIg), although these cells express surface membrane immunoglobulin (SmIg). The present study, in which SmIg and CyIg determinations were performed simultaneously using leukemic B cells from 20 patients with CLL, demonstrates that CyIg staining was detectable in each CLL cell population examined and that the intensity of cytoplasmic immunofluorescent staining in each instance was moderate to strong. Both SmIg and CyIg light chain determinations indicated monoclonality in all 20 cases. The heavy chain class of SmIg and CyIg in each CLL cell population was not uniformly comparable, however. The majority (15 cases) of CLL B cells contained mu heavy chain CyIg and mu and delta heavy chain CyIg was demonstrated in the remaining six cases. In contrast, the SmIg phenotype appeared heterogenous with both gamma and alpha chain determinants found associated with mu or mu and delta chains on the same leukemic cell populations. This apparent polyclonal SmIg staining pattern was most likely due to nonspecific adsorption of the patient's own serum Ig by Fc receptors on CLL B cells. It is concluded that the great majority of CLL B cells contain detectable CyIg and that CyIg determination is superior so SmIg phenotyping in documenting the monoclonality of CLL. (Author abstract) (12 Refs)

43. INCREASE IN THE NUMBER OF LYMPHOCYTES SECRETING IGG FOLLOWING BLOOD TRANSFUSION.

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Blood; 59(2):312-316 1982

A sequential change in the number of circulating immunoglobulin (Ig) secreting cells of each Ig class following blood transfusion was studied using a reverse hemolytic plaque assay. The subjects studied were in two main groups, immunologically normal individuals and patients with malignant lymphoma or multiple myeloma who are presumably, immune incompetent. A consistent increase in circulating IgG-secreting cells, along with either an earlier or simultaneous increase in IgM-secreting cells, was observed following blood transfusion in the immunologically normal individuals. An increase in IgA-secreting cells was also observed, but at a minimal magnitude. Such an increase was not apparent in patients with lymphoma or myeloma. The possible use of blood transfusion as a means of 'challenging and checking' for the state of immune responsiveness in vivo is discussed. (Author abstract) (9 Refs)

44. SELECTIVE DECREASE OF IGE BLOOD LEVEL IN PATIENTS WITH CERTAIN MALIGNANT TUMORS.

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Res. Roentgenoradiological and Oncological Inst., Kiev, USSR
Vrach Delo; (12):90-93 1981

The role of IgE in antitumor immunity was studied in 102 patients with precancerous breast diseases and in 372 patients with breast cancer (168 had Stage I-II, 145 had Stage III, and 59 had Stage IV). The blood levels of IgA, IgM, and IgG were assayed by radial immunodiffusion. The blood level of IgE was determined by radioimmunoassay. The IgM levels in the patients in Stages I-II, III, and IV were 1.1, 1.08, and 1.01 mg/ml, respectively, compared with 1.05 mg/ml in healthy controls and 1.2 mg/ml in the patients with precancerous breast diseases. The blood levels of IgG in patients in Stages I-II, III, and IV were 17.0, 16.6, and 18.7 mg/ml, respectively, compared with 15.3 mg/ml in healthy controls and 16.4 mg/ml in the patients with precancerous conditions. The corresponding levels of IgA were 3.7, 3.7 and 4.4 mg/ml, vs 3.1 and 3.5 mg/ml, respectively. All patients with breast cancer showed marked decrease of IgE level: 18.7 44.6, and 20.4 nanog/ml in Stages I-II, III, and IV, respectively, compared with 202.5 nanog/ml in healthy controls. (3 Refs) (In RUS)

45. ON IMMUNOGLOBULIN HEAVY CHAIN GENE SWITCHING: TWO 5G 12B GENES ARE REARRANGED VIA SWITCH SEQUENCES IN MPC-11 CELLS BUT ONLY ONE IS EXPRESSED.

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Nucleic Acids Res; 10(2):611-630 1982

During B lymphocyte differentiation, switches in the expression of heavy chain immunoglobulin constant region (CH) genes occur by a novel DNA recombination mechanism. We have investigated the requirements of the CH gene switch by characterizing two rearranged gamma2b genes from a gamma2b producing mouse myeloma (MPC-11). One of the two gamma2b genes is present in two-three copies per cell (gamma2b strong hybridizer) while the other is present in approx one copy per cell (gamma2b weak hybridizer). Genomic clones of the gamma2b strongly hybridizing gene indicate that this is an abortive switch event between the Sgamma3 and Sgamma2b regions. However, clones of the gamma2b weakly hybridizing gene suggest a functional rearrangement due to the presence of VH, JH and Smu sequences. The switch-recombination sites of these rearranged gamma2b genes and those of other CH genes show a high degree of preference for the sequence AGGTTG 5' of either the Smu donor site or the appropriate CH S acceptor site. AGGTTG and its analogs are rare in the Smu region, are somewhat prevalent in Salpha and in the case of Smu are found 5' of a tandemly repeated DNA sequence (GAGCT, GGGGT) comprising most of Smu. (Author abstract) (53 Refs)

46. ULTRASTRUCTURAL ANALYSIS OF MEMBRANE-BOUND POLYSOMES IN HUMAN MYELOMA CELLS.

Kitani T, Yonezawa T, Imanaka T, Hiraoka A, Nasu T
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Blut; 44(1):51-63 1982

Counts of ribosomes were determined in membrane-bound polysomes of 75 patients with different M-protein compositions

(44 IgG-, 14 IgA-, 5 IgD-, 2 IgE-myelomas, 1 macroglobulinemia, 9 BJP myeloma). Ultrathin sections (about 50 nanometer) were cut tangentially and were examined by electron microscopy. For each patient 10-15 micrographs (magnification x 10,000) were inspected and 100-200 membrane-bound polysomes of perfect shape were used for the ribosome counts. The curves of ribosome distribution (up to 21 ribosomes) showed two peaks for IgM, a high peak at 7 and a lower peak at 17-18 ribosomes. Peaks were observed at 7 and 13 ribosomes for IgA-, IgD- and IgE myeloma and macroglobulinemia. BJP myeloma showed a sharp peak only at 7 ribosomes. The results suggest that BJP myeloma has only small polysomes participating in light (L) chain synthesis while the other myelomas have large and small polysomes participating in heavy (H)- and L-chain synthesis, respectively. A similar analysis of marrow from a liver cirrhosis patient with marked reactive plasmacytosis showed sharp peaks at 7 and 17 ribosomes, similar to that obtained in the IgG myeloma patients. The present findings in the myeloma patients can be accounted for by structural relationship between immunoglobulins and Bence Jones proteins. The relationship of polysome size to L- and H-chain globulins is discussed. (13 Refs)

47. SIGNIFICANCE OF PREGNANCY-ASSOCIATED ALPHA2-GLYCOPROTEIN (ALPHA2-PAG) IN PATIENTS WITH BREAST, GASTRIC AND COLORECTAL CANCER.

Shimizu Y, Oshima K, Nakano Y, Fujita M, Taguchi T
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Biken J; 24(3):95-102 1981

Pregnancy-associated alpha2-glycoprotein (alpha2-PAG) levels were measured in human sera by a modification of Laurell's electroimmunoassay using rabbit anti-alpha2-PAG serum. Sera were obtained from healthy controls (32 males and 46 females), patients with benign breast diseases (55 cases), and patients with breast (82 cases), gastric (89 cases), or colorectal (22 cases) cancers. In healthy controls, the mean alpha2-PAG value for females was higher than that for males (p less than 0.05), so alpha2-PAG values for males and females were considered separately in this study. Serum alpha2-PAG levels in patients with benign breast tumors were almost the same as those of controls. In patients with primary breast and gastric cancer, alpha2-PAG levels were higher than those of controls (p less than 0.005) and tended to increase with progress of the disease. Raised alpha2-PAG levels decreased in these patients after curative surgery. These results show that serum alpha2-PAG is useful as a marker in both the initial diagnosis and follow-up of breast and gastric cancer. The reliability of alpha2-PAG as a tumor-associated marker was reinforced by comparison of the positive rates of the three parameters alpha2-PAG, cacinoembryonic antigen (CEA), and immunosuppressive acidic protein (IAP) in patients with breast and gastric cancer. (Author abstract) (22 Refs)

48. INDUCTION OF FCRALPHA ON MURINE LYMPHOCYTES BY IGA IN VITRO.

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J Immunol; 128(2):888-894 1982

The regulatory influence of IgA on the expression of Fc receptors specific for IgA (FcRalpha) on mouse spleen cells was studied. In normal BALB/c spleen cells, the proportion of FcRalpha-bearing (FcRalpha+) cells was less than 2%, determined by the rosette formation with IgA-coated sheep red blood cells (SRBC) or with trinitrophenylated (TNP) SRBC after incubation with soluble MOPC 315 IgA, which specifically binds with TNP. There was no marked increase of FcRalpha+ cells after 24-hr culture in IgA-free medium or treatment with acid pH (pH 5.0). When cultured with MOPC 315 IgA for 18 hr, there was a dose-dependent increase of the cells binding TEPC 15 IgA-coated SRBC as well as the cells forming rosettes with TNP-SRBC. Twenty to 30% of spleen cells expressed FcRalpha when cultured with 300 ug/ml IgA. The induced receptors bound both soluble IgA and IgA-coated SRBC, and proved to be specific for IgA by the inhibition with other isotypes. The induction of FcRalpha by IgA was inhibited by the inhibitors of RNA and protein synthesis (actinomycin, puromycin, cycloheximide), and required more than 8 hr of culture for the expression. Mitomycin (50 ug/ml) failed to inhibit the induction, indicating that proliferation of the cells is not required. FcRalpha was induced by dimer IgA but not by monomer IgA. Reduction of IgA with 0.02 M dithiothreitol resulted in the loss of inducing ability. However, reduced IgA competitively inhibited the induction of FcRalpha by nonreduced IgA and cytophilic binding of nonreduced IgA to the receptor. FcRalpha was induced by IgA on spleen cells depleted of adherent cells by Sephadex G-10 column passage. Both T and B lymphocytes were shown to express FcRalpha. (Author abstract) (34 Refs)

49. TISSUE ORIGINS OF HUMAN POLYMERIC AND MONOMERIC IGA.

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J Immunol; 128(2):990-995 1982

Human tissues were examined for their ability to produce monomeric and polymeric forms of IgA in vitro. Mononuclear cells were examined for the presence of cytoplasmic immunoglobulins and J chain (by immunofluorescence) and for the amounts and molecular forms of intracellular and secreted IgA (by radioimmunoassay). Cultured bone marrow cells were the largest producers of total IgA, and approx 90% of the secreted IgA was monomeric. Spleen cells also produced predominantly monomeric IgA. Intestinal lamina propria cells secreted the greatest amounts of polymeric IgA, but also produced significant amounts of monomeric IgA. Tonsillar, lymph node, and peripheral blood cells produced approx equal proportions of monomeric and polymeric IgA. These results suggested that bone marrow may be a major source of serum monomeric IgA, and that lymphoid tissues associated with secretory surfaces may provide a greater proportion of polymeric IgA than other lymphoid tissues. There was a positive correlation between the production of polymeric IgA and the presence of cytoplasmic J chain; tissues that produced predominantly monomeric IgA generally displayed fewer cells containing cytoplasmic J chain. (Author abstract) (35 Refs)

HUMORAL IMMUNE BLOCKING FACTORS AND ANTIGEN-ANTIBODY COMPLEXES

50. IMMUNE COMPLEXES AND CIRCULATING ANTIBODIES AGAINST AUTOLOGOUS LEUKAEMIC CELLS IN PATIENTS WITH ACUTE LEUKAEMIAS.

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Immunology; 45(3):569-575 1982

Serum of patients with different forms of acute leukemias were analyzed either for the presence of circulating antibodies against autologous leukemic cells or for that of soluble immune complexes. At the moment of their diagnosis, 12/25 patients with different types of leukemias, showed circulating serum immunoglobulins capable of binding to the leukemic cell surface (LCS). These ant i-LCS immunoglobulins were of the IgG class and were detectable by a binding assay employing glutaraldehyde-fixed target cells and radioiodinated Staphylococcus aureus Protein A. Their digestion with pepsin showed that the site involved in the binding was in the F(ab')2 fragment. The anti-LCS immunoglobulins were observed in patients with nonlymphatic leukemias but not in the four cases of acute lymphocytic leukemia studied. Forty percent of the patients with anti-LCS immunoglobulins had high levels of circulating immune complexes, detectable by a competitive test with bovine conglutinin and an enzymatically-active antigen-antibody probe. After cytostatic chemotherapy, the level of circulating immune complexes decreased in all the patients, while the anti-LCS immunoglobulins remained constantly detectable and appeared also in those who were negative at the day of the diagnosis. (Author abstract) (36 Refs)

51. CIRCULATING IMMUNE COMPLEXES IN CROHN'S DISEASE. THEIR CHARACTERIZATION AND INTERRELATIONSHIP WITH COMPONENTS OF THE COMPLEMENT SYSTEM.

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Dig Dis Sci; 27(2):129-138 1982

Of the sera from 55 patients with Crohn's disease, 37% showed evidence of anticomplementary activity. C3 and C4 levels were significantly increased in these patients compared with control subjects, although total hemolytic complement levels were normal. C3 inactivation products were demonstrated in 32.9% of serum and plasma samples from 51 patients with CD. This was taken to be evidence of in vivo activation of C3 and the complement system. Activation of the C' system was thought to be caused by circulating immune complexes since evidence of anticomplementary activity could be correlated with incidence of C3 activation. Gel filtration studies carried out on 15 serum samples (13 patients) showing anticomplementary activity showed this activity to be confined to two fractions of mol wt range greater than 10(6) and 2 x 10(5)-10(6) daltons. IgG and IgA were present in both these fractions. As the mol wt of IgG and IgA are lower than the mol wt range of these fractions, it is possible that the immune complexes were composed of IgG and possibly IgA complexed with an antigen. (Author abstract) (26 Refs)

52. SELECTIVE KILLING OF LEUKAEMIA CELLS BY ANTIBODY-TOXIN CONJUGATES: IMPLICATIONS FOR AUTOLOGOUS BONE MARROW TRANSPLANTATION.

Krolick KA, Uhr JW, Vitetta ES
Dept. Microbiology, Univ. Texas Southwestern Medical Sch., Dallas, TX. 75235

Nature; 295(5850):604-605 1982

The recent development of tumor-reactive monoclonal antibodies has stimulated interest in their use in targeting toxic agents to tumor cells. One such approach involves the covalent coupling of tumor-reactive antibodies to the toxic peptide of the plant toxin, ricin. Such conjugates are highly effective in killing various tumor cells in vitro. Here we have used the murine B-cell tumor, BCL, in an adoptive transfer system capable of detecting 1-10 tumor cells, to demonstrate the effectiveness and specificity of an anti-immunoglobulin(Ig)-ricin A chain conjugate in deleting tumor cells from infiltrated murine bone marrow. We report that the transferred cells were able to repopulate the hematopoietic system of lethally irradiated mice and that in most mice the tumor did not recur. We discuss the implications of this approach for autologous bone marrow transplantation following supralethal tumor therapy. (Author abstract) (13 Refs)

53. BRONCHIAL NEOPLASM WITH EOSINOPHILIA.

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Br J Clin Pract; 35(11/12):418-420 1981

Three patients with carcinoma of the lung exhibited significant eosinophilia. A 57-yr-old man with a 8-mo history of malaise, anorexia, and dry cough, presented with a large irregular mass in the right middle lobe. WBC count was 49,700/ul, with 22% neutrophils, 40% eosinophils, and 36% lymphocytes. Sputum cytology revealed suspicious squamous cells.He was treated with a course of radiotherapy. Six mo later the patient died from a pulmonary embolus. A squamous cell carcinoma with definite anaplastic characteristics was found at autopsy. A 57-yr-old man presented with hemoptysis, wt loss, and anorexia. Chest x-rays revealed an irregular mass, emphysema, and cardiomegaly. WBC count was 15,960/ul, with 34% neutrophils, 18% lymphocytes, and 46.6% eosinophils. Localized resection was planned, however, the patient died 2 wk after admission. Autopsy revealed a localized adenocarcinoma and a greatly dilated heart with intercellular edema and hypertrophy. A 62-yr-old man presented with a dry cough and hemoptysis of 6 mo duration. WBC count was 34,000/ul, with 23% neutrophils, 30% lymphocytes, and 46% eosinophils. Anaplastic carcinoma was revealed by biopsy and a course of radiotherapy was administered. The patient was lost to follow-up. In the first two cases, IgG and IgA were raised and there was a high degree of complement conversion, suggesting that complement fixation together with interaction of antibody with tumor antigen might have provoked the eosinophilia. (14 Refs)

54. FEEDBACK REGULATION OF IMMUNE RESPONSES BY IMMUNE COMPLEXES; POSSIBLE INVOLVEMENT OF A SUPPRESSIVE LYMPHOKINE BY FCRGAMMA-BEARING B CELL.

Miyama-Inaba M, Suzuki T, Paku YH, Masuda T
(c/o Masuda) Inst. Immunology Faculty Medicine, Kyoto Univ., Yoshida, Sakyo, Kyoto 606, Japan
J Immunol; 128(2):882-887 1982

Inoculations of antigen-antibody complexes (immune complexes) with the intact Fc portion generates suppressor cells in vivo by binding to FcRgamma on B cells via Fc portions. The cell type responsible for the suppression appears to be B cells bearing FcRgamma. Neither T cells nor macrophages participate in both the inductive and effective phases of this type of regulation. The suppression caused by splenic B cells, previously stimulated with immune complexes in vivo, is mediated by humoral factor(s) released from them. The suppressive factor(s) have H-2 gene product(s) coded by the right-hand side of the H-2 gene complex, but not for FcRgamma themselves or immunoglobulins. It has shared component(s) with suppressive B cell factor (SBF) released from FcRgamma+ B cells stimulated with immune complexes in vitro, and it resembles SBF in its mode of action. These findings indicate that immune complexes, the final products of antibody responses, control the immune responses by stimulating surface FcRgamma on B cells. It is of interest that this type of regulation functions in vivo. (Author abstract) (45 Refs)

HUMORAL IMMUNOSUPPRESSIVE AGENTS

55. ANALYSIS OF ANTIGEN-BINDING CELL SURFACE IG PROFILES AND IG-SECRETING CELLS IN MICE CARRYING THE NU ALLELE: IMMUNE REGULATION ABNORMALITY IN HETEROZYGOUS NU/+ MICE.

Fehniger TE, Martinez-Maza O, Kanowith-Klein S, Ashman RF
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J Immunol; 128(2):568-574 1982

The sheep erythrocyte- (SRC) induced increase in SRC-binding cells (SRC-ABC) and the increased expression of surface IgG seen in +/+ and nu/+ mice was detectable, but much less marked in the nu/nu mouse, suggesting the influence of mature T cells is necessary for antigen to fully induce these two early events in B-ABC. In many studies of the immune function of lymphocytes from athymic (nu/nu) mice, nu/+ littermates have been used as 'immunologically normal' controls. We have found that nu/+ BALB/c mice differ significantly from their normal +/+ syngeneic counterparts in having a more prolonged in vivo immune response to SRC. The difference was evident in the persistence until at least day 12 of higher levels of ABC, especially in those expressing surface IgG, and specific anti-SRC-IgG-secreting cells. At day 5, the nu/+ had more total and specific IgG PFC and fewer total and specific IgM PFC, suggesting a slower IgM to IgG switch. When T cells from SRC-primed +/+ donors were transferred into syngeneic nu/+ recipients, suppression of the day 12 levels of ABC and of both total and specific anti-SRC IgM and IgG PFC was observed. Primed T cells from nu/+ donors could not produce this suppression. Nonspecific IgG PFC induced by SRC were much reduced in nu/+ mice relative to +/+ mice. Together, these data suggest nu/+ mice may be deficient in a T suppressor or suppressor-inducer cell population that normally limits the duration of the in vivo immune response, and also that nu/+ mice may be deficient in the T cell that helps the SRC-induced development of nonspecific PF C. Thus, the nude allele appears not to be entirely recessive. (Author abstract) (34 Refs)

56. BEHAVIORALLY CONDITIONED SUPPRESSION OF A GRAFT-VERSUS-HOST RESPONSE.

Bovbjerg D, Ader R, Cohen N
Center Brain Res., Univ. Rochester, Rochester, NY, 14642
Proc Natl Acad Sci USA; 79(2):583-585 1982

The compound, cyclophosphamide (CY), previously used to condition suppression of humoral immune responses, was used to condition suppression of a graft-vs-host response (GvHR). Female (Lewis x Brown Norway) F1 rats were conditioned by pairing consumption of a saccharin solution with an intraperitoneal injection of CY at 50 mg/kg of body wt 48 days before immunization. On day 0, all animals were injected with a suspension of splenic leukocytes (2 x 10(7) cells per footpad) obtained from female Lewis donors. The regional GvHR was assessed on day 5 by weighing popliteal nodes. Conditioned animals given a single low-dose injection of CY and reexposed to conditioned stimuli had lymph node weights significantly lower than control groups and did not differ from animals given three injections of CY during the ongoing GvHR. The results suggest that conditioned immunosuppression, previously demonstrated in thymus-dependent and thymus-independent humoral immune responses, also affects the popliteal GvHR, a cellular immune response. (Author abstract) (26 Refs)

57. TRANSIENT ANTIBODY DEFICIENCY AND ABNORMAL T SUPPRESSOR CELLS INDUCED BY PHENYTOIN.

Dosch HM, Jason J, Gelfand EW
Div. Immunology, Dept. Pediatrics, Hosp. for Sick Children, Res. Inst., 555 University Ave., Toronto, Ontario M5G 1X8, Canada
N Engl J Med; 306(7):406-409 1982

Abnormal suppressor T cells and hypogammaglobulinemia developed in an 11-yr-old boy given phenytoin for post-traumatic seizures. Symptoms after 12 mo of therapy included generalized edema, a confluent, desquamating erythematous rash over the entire body, generalized lymphadenopathy with tender firm nodes, enlarged liver and spleen, fever, draining ears, diffusely erythematous throat, and greenish sputum. Symptoms disappeared when the drug was withdrawn. (30 Refs)

58. MALIGNANT TUMORS IN KIDNEY TRANSPLANT RECIPIENTS UNDER IMMUNOSUPPRESSIVE THERAPY.

Vollenweider A, Largiader F, Uhlschmid G, Binswanger U, Briner J
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Schweiz Med Wochenschr; 112(4):102-111 1982

Out of 420 kidney transplant recipients at the University Hospital, Zurich, operated on between 1964 and 1978, 23 developed one or more malignant tumors. This corresponds to 5.8% of all patients. They included eight cases of malignant lymphoma (non-Hodgkin), one of subacute myeloid leukemia, one of acute lymphatic leukemia, six skin cancers and nine cancers of internal organs. Thirteen patients died, a figure corresponding to 8% of all deaths after kidney transplantation. Nine of the 10 patients with lymphoma and leukemia died, in 5 cases despite therapy. The response to therapy (radiotherapy and/or chemotherapy) was much poorer than in other patients with comparable tumors and in some patients completely absent. The only surviving patient (malignant lymphoma of the small bowel and the retroperitoneum) was treated by a combination of surgery, radiotherapy and chemotherapy and has had a symptom-free follow-up time of 3 1/2 yr. The six skin cancers (4 of the spinocellular type) was excised. Recurrences were not noted. The visceral carcinomas (2 breast cancers, 1 carcinoma respectively of the pancreas, the rectum, the liver, the kidneys, the renal pelvis, and the urinary bladder, and 1 seminoma) were treated by generally accepted surgical principles as far as treatment of the patients was possible. The breast cancer and seminoma patients have survived thus far without recurrences or metastases. (Author abstract) (36 Refs) (In GER)

59. THE IMMUNOSUPPRESSIVE EFFECT OF MONOCLONAL ANTI-LYT-1.1 ANTIBODIES IN VIVO.

Michaelides M, Hogarth PM, McKenzie IF
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Eur J Immunol; 11(12):1005-1012 1981

Monoclonal anti-Lyt-1.1 alloantibody was produced as tissue culture supernatant and administered to mice. The antibody, given intraperitoneally, resulted in the suppression of all T cell functions studied, but was without direct effect on B cells. Thus, skin and tumor allograft survival was prolonged and there was suppression of the delayed-type hypersensitivity response; T cell help in the anti-sheep red blood cell antibody response, responder cells in the mixed lymphocyte reaction (MLR), leukoagglutinin-responsive cells, cytotoxic T cell (Tc) function and the induction of Tc were either totally or partially suppressed, all these responses being mediated by Lyt-1+2- or Lyt-1+2+ cells in CBA/H mice. By contrast, there was no inhibitory effect on the MLR-stimulating or lipopolysaccharide-responsive cells. The administration of the anti-Lyt-1.1 antibody was accompanied by a depletion of Lyt-1.1+ T cells from both spleen and lymph node. These studies indicate that the monoclonal anti-Lyt1.1 antibody is active in vivo with a selective effect on T cells. The results also have important implications for studies of T cell interactions in the mouse in vivo, and for similar studies in man. (Author abstract) (26 Refs)

OTHER RELATED STUDIES

60. PSEUDOLYMPHOMAS OF THE STOMACH: A LESION CHARACTERIZED BY PROGRESSIVELY TRANSFORMED GERMINAL CENTRES.

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Histopathology; 6(1):61-68 1982

Eleven cases of pseudolymphoma of the stomach are described with differential diagnostic features; tumor histopathological characteristics and circumstances which may lead to their development are discussed. From all fixed blocks, hematoxylin-eosin, PAS-hematoxylin, methylated Giemsa and reticulin stained sections were examined. In some cases, the naphthol-AS-DR chloroacetate esterase reaction was also used. The immunoperoxidase method was used to demonstrate intracellular immunoglobulins. Antihuman IgM, IgG, IgA, kappa and lambda peroxidase-labeled antisera were obtained. Antimuramidase (antilysozyme), anti-human IgD and J-chain antibodies were applied using the peroxidase-antiperoxidase method. In two cases in which fresh tissue was available, cryostat sections were prepared and treated with sheep RBCs covered with antibody and complement-EAC-RBC. Of the 11 patients (5 men, 6 women; av 56 yr old), 7 had clinical diagnoses of early or ulcerated cancer and 3 had clinical diagnoses of chronic gastric ulcer and suspicion of malignancy. Chronic peptic ulcer was the most frequent cause of reactive, hyperplastic changes; progressive alteration of the follicle, ie the progressively transformed germinal center, was a frequent lesion. Three Types (1, 2, and 3) of histological pattern were identified by examination of the sections. Typical follicular hyperplasia (Type 1), the larger follicles with small germinal centers (Type 2), and the very large follicle-like structures without germinal centers (Type 3), were evidently subsequent phases in the development of a single lesion. Demonstration of the large follicles, together with a polyclonal nature of plasma cells, was thought to be important in excluding suspicion of malignancy. (21 Refs)

61. IMMUNOCHEMICAL AND FUNCTIONAL ANALYSIS OF IA-LIKE ANTIGENS ON HUMAN MONOCYTE-MACROPHAGES WITH MONOCLONAL ANTIBODIES.

Ng AK, Zhang YH, Russo C, Ferrone S
Dept. Pathology, Columbia Univ., 630 W. 168th St., New York, NY, 10032
Cell Immunol; 66(1):78-87 1982

The distribution, structural profile, and functional properties of Ia-like antigens synthesized by human monocyte-macrophages have been analyzed using monoclonal antibodies to common determinants of these antigens. Up to 45 and 70%- of monocyte-macrophages isolated from the fluid of blisters induced with cantharidin and from peripheral blood, respectively, react with monoclonal antibodies to human Ia-like antigens. The level of Ia-like antigens on monocytes-macrophages appears to be similar to that on cultured B lymphoid cells. Monoclonal antibodies to common determinants of Ia-like antigens specifically block antigen presentation by monocyte-macrophages to T lymphocytes as well as proliferative response to T lymphocytes to autologous and allogeneic monocytes-macrophages. These results indicate that common determinants of Ia-like antigens play a role in the interaction of monocytes-macrophages with T lymphocytes. (Author abstract) (28 Refs)

62. B CELL, HELPER T CELL, AND SUPPRESSOR T CELL ABNORMALITIES CONTRIBUTE TO DISORDERED IMMUNOGLOBULIN SYNTHESIS IN PATIENTS FOLLOWING BONE MARROW TRANSPLANTATION.

Korsmeyer SJ, Elfenbein GJ, Goldman CK, Marshall SL, Santos GW, Waldmann TA
Metabolism Branch, NCI, NIH, Bethesda, MD, 20205
Transplantation; 33(2):184-190 1982

The pathogenic mechanisms responsible for the hypogammaglobulinemia that occurs in patients who have undergone bone marrow transplantation were studied using peripheral blood lymphocytes in an in vitro immunoglobulin biosynthesis assay. None of the nine marrow recipients between 2 and 15 mo after transplantation produced normal amounts of IgG, IgA, or IgM in response to pokeweed mitogen (a T cell-dependent activator). However three of these same patients responded to Epstein-Barr virus (a helper T cell-independent activator), suggesting that these possessed responsive B cells. Cocultures of the marrow recipients' lymphocytes with lymphocytes from their respective donors or other normal subjects documented excessive suppressor cell activity in five cases. These suppressor cells frequently had profound activity (greater than 80% suppression of the immunoglobulin synthesis of cocultured normal cells), were predominantly radioresistant, and were T cells in the cases where analyzed. Helper T cell activity for immunoglobulin synthesis was not demonstrable in seven of the nine cases. In addition, four of the patients apparently possessed defective B cells. Although most patients had combined defects of several lymphocyte subpopulations, it appeared that either an isolated helper T cell or isolated B cell deficiency was sufficient to result in altered Ig synthesis. In this regard, two patients had demonstrable helper T cell defects with partially responsive B cells and no excessive suppressor activity. Interestingly, these two patients were experiencing a recurrence of their hypogammaglobulinemia following a period of normalized immunoglobulin levels. Thus, defects within all lymphocytic elements involved in the response and regulation of immunoglobulin synthesis were identified and may contribute to the humoral immunodeficiency which follows marrow transplantation. (Author abstract) (25 Refs)

63. IMMUNOLOGICAL SUBSETS IN HUMAN B-CELL LYMPHOMAS.

Godal T, Lindmo T, Marton PF, Landaas TO, Langholm R, Hoie J, Abrahamsen AF

Lab. Immunology, Norwegian Radium Hosp., Montebello, Oslo 3, Norway

Scand J Immunol; 14(5):481-492 1981

Fifty human B-cell lymphomas have been studied with regard to surface markers (surface immunoglobulins (sIg) and complement receptors (CR)), capping of sIg, and relative amounts of sIg by single-cell flow cytometry. The results show that these lymphomas can be subdivided into distinct immunological subsets. Whereas one histological subgroup (lymphocytic) consisted of only one immunological subtype, others were heterogeneous with regard to immunological subtypes. This was most striking in nodular lymphomas of germinal center cell origin (centroblastic/centrocytic). Our studies provide further evidence for the existence of a large number of subsets in the B-cell compartment of the immune system. sIgD was only found in association with sIgM. The relative amounts of sIgD varied, especially in nodular lymphomas. A discrepancy between capping of sIgM and sIgD was also found in some lymphomas belonging to this group. These findings together with other observations suggest that sIgD plays a role in B-cell maturation and differentiation events taking place in germinal centers and becomes lost during this process. A close association was found between the presence of CR and capping of sIgM but not capping of sIgD or sIgG. Nodular lymphomas expressing sIgG only, lacked CR. These findings suggest that CR may become lost during maturation and differentiation processes also taking place in germinal centers. Lymphoplasmacytoid lymphomas, which show morphological evidence of differentiation towards plasma cells, could be subdivided into three immunological subsets, indicating that plasma cell maturation may take place from different subsets of B cells. (Author abstract) (39 Refs)

64. EFFECT OF COLONY STIMULATING FACTOR ON MURINE MACROPHAGES. INDUCTION OF ANTITUMOR ACTIVITY.

Wing EJ, Waheed A, Shadduck RK, Nagle LS, Stephenson K

Dept. Medicine, Univ. Pittsburgh Sch. Medicine, Pittsburgh, PA, 15213

J Clin Invest; 69(2):270-276 1982

Colony stimulating factor (CSF) was assessed for its capacity to stimulate antitumor activity in macrophages. Murine peritoneal macrophages incubated with CSF for 48 hr inhibited [3H]thymidine (TdR) incorporation by P815 tumor cells to approx 20% of control values. Inhibition of CSF-stimulated macrophages was significantly greater than inhibition by unstimulated macrophages (p less than 0.001). CSF had little direct effect on the proliferation of either tumor cells or macrophages alone, indicating that the antitumor activity of CSF was mediated by macrophages. It is unlikely that impurities in the CSF preparations were responsible for the effect since CSF that had been purified to homogeneity was as active as crude preparations. Furthermore the activity of CSF on macrophages was blocked by addition of purified anti-CSF antibodies. In addition to being tumoristatic, CSF-stimulated macrophages were tumoricidal as determined by a tumor colony growth assay. Tumor cells that had been incubated with CSF-stimulated macrophages showed a significant reduction in tumor colony-forming units (p less than 0.01). Thus, in addition to its effect on hemopoietic stem cells, CSF induces certain effector functions in mature macrophages that may enhance endogenous antitumor host defenses. (Author abstract) (21 Refs)

65. MONOCLONAL ANTIBODIES TO THE HUMAN MAMMARY GLAND. I. DISTRIBUTION OF DETERMINANTS IN NON-NEOPLASTIC MAMMARY AND EXTRA MAMMARY TISSUES.

Foster CS, Edwards PA, Dinsdale EA, Neville AM

Ludwig Inst. Cancer Res., Royal Marsden Hosp., Sutton, Surrey SM2 GPX, England

Virchows Arch [Pathol Anat]; 394(3):279-293 1982

Mouse monoclonal antibodies have been raised to the human milk fat globule membrane. The distribution of the antigens detected by four of the antibodies has been examined in formalin-fixed, paraffin-embedded human tissues by light microscopic immunocytochemistry. The four antibodies stain lactating breast and normal resting breast. Two exclusively stain the luminal membranes of breast epithelial cells. A third antibody stains in addition the lateral membranes of duct epithelial cells. The fourth antibody stains both epithelial and myoepithelial cells. None of the antibodies is breast specific, nor do they stain every epithelial cell within the breast. Instead, each antibody reveals a complex and heterogeneous distribution of staining throughout the normal tissues. Within the breast, the staining by a given antibody is usually segmental and conforms to secretory units and their associated ducts. Similarly heterogeneous patterns of staining are also observed in the extramammary normal tissues. Despite the apparent morphological identity between breast epithelial cells when examined by conventional light microscopy, the hitherto unrecognized 'functional' heterogeneity, which as been revealed by the monoclonal antibodies could have importance in understanding the biology of the normal breast and the pathology of breast cancer. (Author abstract) (18 Refs)

66. ISOLATION OF ALPHA-FETOPROTEIN MESSENGER RIBONUCLEIC ACID FROM AH-66 ASCITES HEPATOMA CELLS.

Choi NH, Higashi T
Dept. Biochemistry, Sch. Pharmaceutical Sciences, Showa Univ., 1-5-8, Hatanodai, Shinagawa-ku, Tokyo, 142, Japan
Chem Pharm Bull (Tokyo); 29(11):3303-3310 1981

The messenger (m)RNA for alpha-fetoprotein (AFP) was isolated from polysomes of AH-66 rat hepatoma cells by extraction of immunoprecipitates and purification by affinity chromatography with oligo(deoxythymidine)-cellulose column. Sodium dodecyl sulfate polyacrylamide gel electrophoresis of AFP gave two mol wt peaks of 72,000 and 74,000; the purified AFP contained 1.5% hexose, 1.5% hexosamine, and 0.9% sialic acid. Electrophoresis of purified AFP mRNA on acid-urea agarose gel suggested a mol wt of 2,700. Purified anti-AFP antibody from anti-rat AFP horse antiserum was reactive against AH-66 ascites fluid, purified rat AFP, and anti-horse IgG rabbit antibody, but not adult rat serum. A quantitative analysis showed that the molar ratio of anti-AFP antibody to rat AFP is approx one at the equiva lent point. Purified AFP mRNA translated in the wheat germ S-30 cell-free system was measured by radioactivity incorporated in immunoprecipitates; results indicated that the obtained AFP mRNA was at least 75% pure in terms of messenger activity. (21 Refs)

67. MEDICAL PROBLEMS IN HOMOSEXUAL MEN.

Dritz SK
No affiliation given
West J Med; 136(1):54-55 1982

A newly reported medical problem of young, previously healthy homosexual men, is the occurrence of Pneumocystis carinii pneumonia and Kaposi's sarcoma. In contrast to the indolent course of Kaposi's sarcoma in aged Africans or patients receiving immunosuppressive therapy, the disease sometimes has a fulminating course in homosexual men. Suspected interrelationships (possibly on a genetic level) of Epstein-Barr virus, cytomegalovirus, and perhaps some local peculiarities of this population's life style may be involved. Another medical problem of homosexual men is infected traumatic, amebic, or herpetic ulcerations of the rectal mucosa, which may be mistaken for rectal carcinoma. (3 Refs)

68. SYMPOSIUM ON TUMOURS IN THE TROPICS: HISTORICAL INTRODUCTION, BURKITT'S LYMPHOMA, NASOPHARYNGEAL CARCINOMA AND KAPOSI'S SARCOMA.

Hutt MS
Geographical Pathology Unit, Dept. Histopathology, St. Thomas' Hosp. Medical Sch., London SE1 7EH, England
Trans R Soc Trop Med Hyg; 75(6):761-765 1981

The geographic distribution of Burkitt's lymphoma (BL) in Africa and New Guinea can be explained by its association with endemic malaria. Heavy Plasmodium falciparum infection in young children suppresses the immune system and enhances lymphocyte proliferation, which in turn may enhance susceptibility to the oncogenic effects of the Epstein-Barr virus (EBV). The age at the time of EBV infection and genetically determined immunologic deficits may also be involved. The sporadic BL of Western nations is usually not associated with EBV. EBV is also implicated in nasopharyngeal carcinoma (NPC). Most of the high-NPC areas are in the tropics of Africa and Asia. Genetic factors seem to be involved. In Malaysia, Singapore, and Hong Kong, the NPC frequency is high in Malays and ethnic Chinese, but low in Indians. Chinese patients with NPC have a previously unidentified second-locus HLA antigen (Sin-2). The NPC frequency is also high among Eskimos, Aleuts, and Alaskan Indians. In this population, the BW40 component of the HLA system is more frequent in NPC patients than in other groups. Kaposi's sarcoma (KS) is rare everywhere in the world except among the black populations of tropical Africa. Its geographic distribution does not seem to be related to ethnic origin, suggesting that environmental factors are the major etiologic determinant. Endogenous, perhaps hormonal factors might account for the male preponderance among KS patients. European and American cases of KS have been reported in immunosuppressed patients. An association of KS with elevated cytomegalovirus antibody titers has been reported in Western countries but not in Africa. (78 Refs)

69. OT-CLL: A HUMAN T CELL CHRONIC LYMPHOCYTIC LEUKEMIA THAT PRODUCES IL 2 IN HIGH TITER.

Friedman SM, Thompson G, Halper JP, Knowles DM
Div. Rheumatology, Dept. Medicine, Columbia Univ. Coll. Physicians and Surgeons, New York, NY, 10032
J Immunol; 128(2):935-940 1982

This report identifies and describes a human T cell chronic lymphocytic leukemia, OT-CLL, which can be triggered by selected mitogens (either PHA or Con A) to produce IL 2 in high titer. Optimal IL 2 production requires culturing OT-CLL cells at 2 to 5 x 10(6)/ml for 24 hr in the presence of 1 to 2% PHA-M. Under these conditions, the titer of IL 2 generated is greater than 20-fold that obtained from conventional sources, eg, from mitogen-activated tonsillar lymphocytes. Two lines of experimental evidence suggest that the tumor cell product(s) is IL 2. First, in functional assays, supernatants derived from cultures of PHA-activated OT-CLL cells trigger the proliferation and long-term growth of IL 2-dependent human TCL cells. Second, a partial biochemical purification of the active moiety(ies) derived from OT-CLL demonstrates marked similarity to conventional human IL 2. Thus, the biologically active material(s) precipitates in 50 to 70% saturated (NH4)2SO4 solutions; elutes from DEAE-Sepharose in the presence of 0.04-0.08 M NaCl; and has an apparent mol wt of approx 14,000, as determined by Sephadex G-100 gel filtration. In addition, analysis of OT-CLL cells by indirect immunofluorescence, utilizing a panel of monoclonal antibodies, confirms not only that these tumor cells are of T cell lineage but that they display surface antigens that define the normal human peripheral T cell subset subserving helper or inducer function: OKT3+, OKT4+, OKT8-. (Author abstract) (36 Refs)

70. TNP-MODIFIED SYNGENEIC CELLS ENHANCE IMMUNOREGULATORY T CELL ACTIVITIES SIMILAR TO ALLOGENEIC EFFECTS.

Eastman AY, Lawrence DA
Dept. Microbiology and Immunology, Albany Medical Coll., Union Univ., Albany, NY, 12208
J Immunol; 128(2):926-931 1982

The ability of TNP-modified syngeneic B cells (TNP-B cells) to alter unprimed T cell regulation of in vitro humoral immune responses to sheep erythrocytes was examined. High doses of T cells (greater than 10(6)) suppressed TNP-B cell activation, and irradiation of the T cells (1000 R) abolished this suppression, revealing a significant degree of radioresistant help in the T cell preparations. Similarly, help was enhanced when the T cells were irradiated and co-cultured with semiallogeneic B cells (Allo-B cells). T cells (less than 10(6)) pretreated with mitomycin C provided a greater degree of help to both TNP-B cells and Allo-B cells than the untreated T cells; however, significant mitomycin C-resistant suppression was apparent with higher doses of T cells. In contrast to T cell regulation induced by TNP-B cells and Allo-B cells, help provided to unmodified syngeneic B cells was of lower magnitude and was relatively sensitive to irradiation and mitomycin C treatment, and suppressor activities were not as apparent. In 'bystander' and 'membrane-segregated' cultures TNP-modified B cells also augmented T cell activities with features similar to those stimulated by allogeneic cells: (i) Irradiated, TNP-modified stimulator cells induced a significant degree of bystander help that was radioresistant. Allo-B cells also enhanced bystander help, although significant bystander suppressive effects also were apparent with high T cell doses. (ii) The helper activity induced by TNP-B cells and Allo-B cells was mediated primarily by diffusible factors, and the production of the factors was radioresistant. (iii) The release kinetics of the helper factors were similar, in that optimal helper activity was observed by 48 hr. In contrast, factor-mediated help observed with unmodified syngeneic cells was minimal and attained optimal levels at 72 to 96 hr. In conclusion, TNP-modified syngeneic B cells stimulated T cell activities, leading to the enhancement of nonantigen-specific help and suppression with characteristics similar to positive and negative allogeneic effects, respectively. This study indicates that immunoregulatory T cell function can be modulated by self-altering agents. (Author abstract) (40 Refs)

71. EFFECT OF ESTRADIOL AND DEGREE OF CELL DIFFERENTIATION ON HUMAN MELANOMA SUSCEPTIBILITY TO KILLING BY MONOCLONAL ANTIBODIES.

Hakim AA

Dept. Oral Diagnosis, Coll. Dentistry and Basical Medical Sciences, Univ. Illinois, 180 Longwood Drive, Kankakee, IL, 60901

Immunol Lett; 4(1):59-64 1982

The relationship of antigenic determinants of melanotic and amelanotic human malignant melanoma cells to responsiveness to estradiol (ES) was studied. Cultures grown in the absence and presence of ES were used to develop various cell lines: a non-responsive melanotic (E-M+ShA) was derived from ES-responsive melanotic (E+M+ShA) and an ES-responsive amelanotic (E+M-SR) was derived from ES-non-responsive amelanotic (E-M-SR). Cellular responsiveness to hormone was determined by incubation with insulin, with addition of (3H)thymidine after 72 hr. Spleen lymphocytes from mice preimmunized with E+M+ShA, E-M+ShA, E-M-SR, and E+M-SR were fused with murine non-producer myeloma cells to obtain mouse-mouse hybridoma cultures synthesizing monoclonal antibodies against human malignant melanoma. Complement-dependent cytotoxic activity of the monoclonal antibodies varied from one hybridoma to another. Results indicate that the antigenic determinants of melanoma cells vary from one cell line to another; efficiency of complement-mediated killing is a function of responsiveness to estradiol and degree of melanogenesis. (37 Refs)

72. HUMORAL FACTORS INVOLVED IN THE MECHANISM OF REACTIVITY OF THE MICROPLATE LEUKOCYTE ADHERENCE INHIBITION ASSAY.

Russo AJ, Howell JH, Goldrosen MH

Dept. Surgical Oncology, Tumor Immunology Group, Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263

Immunol Commun; 10(7):611-630 1981

To study if specific antigen(s)-induced adherence inhibition is due to direct cell contact or mediated by a soluble factor, spleen cells and enriched populations of B-cells and T-cells from normal C57Bl/6J mice and mice bearing progressively growing MCA-38 tumors were incubated with MCA-38 tumor antigen(s) and control B-16 melanoma antigen(s) for 1 hr at 37 C. The supernatants of these cultures were harvested and evaluated for their ability to induce adherence inhibition of normal peritoneal cells. Supernatants of MCA-38 sensitized B-cells but not T-cells could induce adherence inhibition of normal peritoneal cells. Furthermore, supernatants of MCA-38 sensitized spleen cells could not induce adherence inhibition of normal peritoneal cells, despite the fact that these cells can directly undergo specific antigen(s)-induced adherence inhibition. However, the sensitized spleen cells, after removal of the supernatant, were less adherent than comparable cells incubated with media alone, suggesting that the reactive cell within the spleen cell population adsorbed the soluble mediator as it was being generated. Affinity chromatography studies revealed that the biologically active soluble mediator contained IgG. Gel filtration studies indicated that the soluble mediator had a mol wt greater than 190,000 daltons. Thus, in this murine tumor model, leukocyte adherence inhibition is dependent upon the interaction between sensitized B-cells and specific tumor antigen(s) to produce a soluble mediator and is an antibody-mediated phenomenon. (Author abstract) (19 Refs)

73. BIOLOGY OF SIMIAN VIRUS 40 (SV40) TRANSPLANTATION ANTIGEN (TRAG). VIII. RETENTION OF SV40 TRAG SITES ON PURIFIED SV40 LARGE T ANTIGEN FOLLOWING DENATURATION WITH SODIUM DODECYL SULFATE.

Flyer DC, Tevethia SS

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Virology; 117(1):267-270 1982

Simian virus 40 (SV40) large tumor (T) antigen was isolated from SV40-infected permissive and -transformed cells by immunoprecipitation with anti-T sera and purified by electrophoresis on solubilizable SDS-polyacrylamide gels. This method proved to be a rapid and efficient procedure for purifying T antigen as 74% of the immunoprecipitated T antigen was subsequently recovered. The purified , SDS-denatured large T antigen retained its ability to react with anti-T antibody and to immunize mice against a challenge of syngeneic SV40 tumor cells, indicating that the antigenic sites present on the large T antigen molecule that induce a tumor rejection response in vivo are resistant to denaturation by SDS. (Author abstract) (25 Refs)

74. THE PROTEIN BINDING OF METHOTREXATE IN THE SERUM OF PATIENTS WITH NEOPLASTIC DISEASES.

Steele WH, Lawrence JR, Stuart JF, McNeill CA
Dept. Therapeutics and Clinical Pharmacology, Univ. Medical Buildings, Foresterhill, Aberdeen AB9 2ZD, Scotland

Cancer Chemother Pharmacol; 7(1):61-64 1981

Binding of serum proteins by methotrexate (MT) was studied in 14 patients (40-80 yr old, av age 61.79 yr) with various malignant diseases (including carcinoma of the breast, lung, cecum, lip, or ovary, brain tumor, osteosarcoma, melanoma, and lymphoma) and in 8 age- and sex-matched controls with nonmalignant conditions (diabetic hypertension, cerebrovascular accident, celiac, or angina). Serum albumin concentrations were measured by the bromocresol green method, MT concentrations by double-antibody radioimmunoassay, and MT-protein interactions by continuous ultrafiltration. At an MT concentration of 50 umole/liter (um/l) mean protein binding (MPB) was 92.04% in controls and 92.77% in cancer patients. Protein binding was reduced in one control (82.97%) and one cancer patient (81.10%), both of whom had reduced serum albumin. Analysis of binding plots for controls and cancer patients indicated no significant differences in MPB. Both groups apparently carried two types of binding sites: a high-affinity, low-capacity type and a low-affinity, high-capacity type. At MT concentrations above 50 um/l, binding of protein by MT decreased and levels of free MT increased, both in nonlinear fashion. Since pharmacological and toxic effects of MT depend on free drug levels, results indicate that the effects of albumin levels and nonlinear protein binding at high MT levels should be taken into account when planning high-dose MT therapy. (19 Refs)

75. UNIFORM NOMENCLATURE FOR MONOCLONAL ANTIBODIES DIRECTED AGAINST VIRUS-CODED PROTEINS OF SIMIAN VIRUS 40 AND POLYOMA VIRUS.

Crawford L, Harlow E
Molecular Virology Lab., Imperial Cancer Res. Fund, Lincoln's Inn Fields, London WC2A 3PX, England

J Virol; 41(2):709 1982

A uniform nomenclature has been agreed upon for monoclonal antibodies directed against virus-coded proteins of simian virus 40 and polyoma virus. Blocks of numbers from PAb1 to PAb999 have been allocated to workers involved in the isolation of monoclonal antibodies of this type. The correspondence between PAb numbers and previously used names is given. (Author abstract) (6 Refs)

76. THE SAME GENETIC LOCUS DIRECTS DIFFERENTIATION-LINKED EXPRESSION OF ENDOGENOUS RETROVIRUS GP70 ON THYMOCYTES AND SPLEEN CELLS IN THE MOUSE.

Tung JS, Shen FW, Viamontes G, Palladino M, Fleissner E
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021

Immunogenetics; 15(1):103-108 1982

Expression of the major envelope glycoprotein (gp70) of murine leukemia virus (MuLV) was studied in spleen cells of C57BL/6 (B6) and 129 mice that are negative for thymocytes surface antigen (GIX) and spleen cells of their congeneic GIX+ and GIX- derivatives. Proteins with a mol wt of approx 70,000 daltons were specifically recognized by a group-specific anti-gp70 serum in spleen cell lysates of 129, B6, and B6-GIX+ mice; 129-GIX- cells were negative. A monoclonal antibody specific for GIX+ MuLV gp70 precipitated the same gp70 molecules on spleen cells from the GIX+ strains. Occurrence of spleen cell gp70 in these strains appeared to controlled by the same genetic locus (Gv-1) that determines the presence of GIX+ gp70 on thymocytes. The presence of gp70 on spleen cells from B6-nu mice as well as on cytotoxic spleen T cells indicated that gp70 molecules are expressed by both T and non-T cells. (15 Refs)

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IMMUNOBIOLOGY AND CANCER

Antibodies and Humoral Immunity

SERIES CB08 No. 82/08

AUGUST, 1982

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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HE 20.3173/2:

TUMOR ANTIBODY PRODUCTION/ CHARACTERIZATION/ DETECTION

1. NATURAL ANTIBODIES TO THE STRUCTURAL CORE PROTEIN (P24) OF THE HUMAN T-CELL LEUKEMIA (LYMPHOMA) RETROVIRUS FOUND IN SERA OF LEUKEMIA PATIENTS IN JAPAN.

Kalyanaraman VS, Sarngadharan MG, Nakao Y, Ito Y, Aoki T, Gallo RC
(c/o Gallo) Lab Tumor Cell Biology, NCI, NIH, Bethesda, MD, 20205
Proc Natl Acad Sci USA; 79(5):1653-1657 1982

We investigated the involvement (in adult T-cell leukemias and lymphomas) of the human T-cell leukemia virus (HTLV) that was previously isolated in one of our laboratories from cultured T cells of some patients in the United States with leukemias and lymphomas involving relatively mature T cells. High titers of antibodies capable of quantitative precipitation of 125I-labeled p24, a well characterized core protein of HTLV, were detected in 12 of 12 patients with untreated adult T-cell leukemia (ATL). (1 negative was a patient on chemotherapy). Ten of the 12 positive samples were from an area where the disease is endemic. Strong precipitating antibodies were also detected in five of seven cases of T-cell malignant lymphoma (TML) which differs from ATL by having fewer leukemic cells in the peripheral blood. High antibody titers were also observed in one of five cases of acute monoblastic leukemia and one of eight cases of chronic myelogenous leukemia in the blast phase of the disease. Low to moderate titers of antibodies were detected in several categories of leukemia (2 cases of blast-phase chronic myelogenous leukemia, 2 cases of acute lymphoblastic leukemia of the null-cell type, and 1 case of acute myelogenous leukemia). Among all categories of leukemias, except ATL and TML, more cases were negative than positive for anti-p24 activity. All of 79 sera from normal Japanese, including 39 collected from the endemic ATL area of southwest Japan, were negative for antibodies to HTLV p24. All the positive reactivities observed were highly specific to HTLV. The only competition observed in the precipitation of HTLV p24 was with HTLV or with cell lines expressing HTLV and not with various animal retroviruses or a large number of human and subhuman primate cell lines, not known to be producing HTLV. The data strongly indicate an association of HTLV with the increased incidence of ATL in parts of Japan, probably with other forms of leukemias in Japan, and, less commonly, with certain T-cell malignancies in the United States. (26 Refs)

2. IDENTIFICATION OF TWO CLASS I ANTIGENS CODED BY THE MAJOR HISTOCOMPATIBILITY COMPLEX OF THE RAT BY USING MONOCLONAL ANTIBODIES.

Misra DN, Noeman SA, Kunz HW, Gill TJ
Dept. Pathology, Univ. Pittsburgh, Sch. Medicine, Pittsburgh, PA, 15261
J Immunol; 128(4):1651-1658 1982

Hybridomas secreting antibodies to rat RT1 class I antigens were produced by fusing lymphocytes from WF rats immunized against the DA strain with P3-653 myeloma cells. Many clones were generated, and five of them -3-1-3(B-1), 3-3-56(A-24), 3-3-60(C-14), 2-5-118(A-2), and 2-1-155(G-4) - were characterized. All five antibodies reacted with RBC having RT1 haplotypes a, b, d, e, f, m, and o. Absorption of the five antibodies with RBC carrying the a, b, d, m, or o haplotypes removed all of the reactivity from each of them. However, competitive inhibition studies separated their specificities into three different types: 118 was unique; 3, 56, and 60 had similar reactivities, and 155 inhibited the reactivity of each of the four. The SDS-PAGE analysis of the antigen(s) precipitated by these antibodies and by the WF anti-DA alloantiserum from NP-40 extracts of 35S-methionine-labeled DA lymphocytes or 125I-labeled DA RBC showed the 45,000-mw component of Class I antigens. The 12,000-mw component was visible with the metabolically labeled samples only. Antibody 118 precipitated a discrete antigen, and the other four antibodies and the alloantiserum precipitated more antigen(s) from the sample that was first immunodepleted completely with antibody 118. The results of direct cellular radioimmunoassay at saturation and of immunoprecipitation at equivalence showed that the amounts of the antigen(s) reactive with the antibodies 3, 56, 60, and 155 and the alloantiserum with respect to that reactive with the antibody 118 were approx twofold greater (antibodies 3, 56, and 60) and five to sixfold greater (antibody 155 and the WF anti-DA alloantiserum). These results demonstrate the presence of at least two class I molecules coded by the major histocompatibility complex of the rat, and they suggest that there is also a third one. (Author abstract) (37 Refs)

3. MONOCLONAL ANTIBODIES RECOGNIZING TUMOR-ASSOCIATED ANTIGEN OF HUMAN OVARIAN MUCINOUS CYSTADENOCARCINOMAS.

Bhattacharya M, Chatterjee SK, Barlow JJ, Fuji H
Dept. Gynecologic Oncology, Roswell Park Memorial Inst., Buffalo, NY, 14263
Cancer Res; 42(5):1650-1654 1982

Spleen cells from BALB/c mice immunized with human ovarian cystadenocarcinoma extract were fused with the mouse myeloma cell line P3/NSI/1-Ag 4 in the presence of polyethylene glycol (Mr 4,000). Of the 46 hybrids obtained, four secreted antibodies preferentially reactive to the immunizing ovarian tumor extract. Two of these hybrids, which showed no reaction with normal controls, were selected for cloning by the limiting dilution method. The numerous clones obtained from each hybrid were screened against a panel of five ovarian tumor extracts, pooled normal ovary extracts, and pooled normal human sera. One clone from each hybrid that showed specificity for ovarian mucinous cystadenocarcinomas was recloned to assure monoclonality and to establish a permanent hybridoma cell line. The antibodies secreted by these cell lines were of IgG1 subclass with kappa light chains. These antibody-producing hybridomas were selected for further analysis of the antibody specificity by a solid-phase radioimmunoassay and quantitative absorption tests. The antigenic determinant recognized by these monoclonal antibodies was unrelated to carcinoembryonic antigen, normal glycoprotein, normal human serum components, or human ABO blood group materials. These antibodies, which have relatively high affinity and can be produced in large amounts, will be useful for the isolation and immunochemical characterization of this antigen. The purified antigen and the sp ecific antibodies could be then combined in a sensitive radioimmunoassay for the early detection of the antigen in the sera and body fluids of patients with ovarian mucinous cystadenocarcinomas. (21 Refs)

4. MONOCLONAL ANTIBODY AGAINST A MEMBRANE ANTIGEN CHARACTERIZING LEUKEMIC HUMAN B-LYMPHOCYTES.

Forster HK, Gudat FG, Girard MF, Albrecht R, Schmidt J, Ludwig C, Obrecht JP
Pharma Res. Div., F. Hoffmann-La Roche and Co., Ltd., Basel, Switzerland
Cancer Res; 42(5):1927-1934 1982

In the diagnosis of non-Hodgkin's lymphomas, the ready characterization of the neoplastic cell lineage by analysis of cell surface markers is of great importance. We present evidence for the existence of a human B-leukemia-associated antigen recognized by a complement-fixing monoclonal antibody (anti-Y 29/55). A hybridoma was produced by fusing mouse myeloma cells and splenocytes of a mouse immunized against lymphoid cells of a patient with B-cell chronic lymphocytic leukemia. Characterization of anti-Y 29/55-reactive normal and malignant leukocytes was demonstrated by cytolysis and indirect immunofluorescence. This revealed reactivity with an antigen on B-lymphoma cells (11 patients), on leukemic lymphocytes in B-cell chronic lymphocytic leukemia (13 patients), and on malignant cells in hairy-cell leukemia (2 patients) but not on leukemic cells of T-cell acute lymphoblastic leukemia (1 patient), on T-lymphoma cells (1 patient), on cells of acute myeloblastic leukemia (4 patients), or of chronic myeloid leukemia (4 patients). No specific cytolysis occurred with B- and T-peripheral blood lymphocytes from (a) healthy donors (16 individuals), (b) patient with reactive lymphocytosis (1 patient), (c) nonleukemic multiple myeloma (6 patients), or (d) Hodgkin's disease (3 patients). Surface immunoglobulin-positive, sheep RBC-negative lymphocytes isolated from human spleen (3 individuals), tonsils (7 individuals), and lymph nodes (1 individual), however, we recognized. It is concluded that leukemic B-cells carry a marker characteristic of nonrecirculating sessile B-lymphocytes. (Author abstract) (54 Refs)

5. DEVELOPMENT OF AN ANTIBODY TO ACTINOMYCIN D AND ITS APPLICATION FOR THE DETECTION OF SERUM LEVELS BY RADIOIMMUNOASSAY.

Brothman AR, Davis TP, Duffy JJ, Lindell TJ
Dept. Pharmacology, Arizona Health Sciences Center, Tucson, AZ, 85724
Cancer Res; 42(3):1184-1187 1982

An antibody specific for actinomycin D (Act D) has been developed and used in a rapid, sensitive radioimmunoassay for detection of this anticancer drug in serum. The 2-amino group of the heterocyclic chromophore of Act D was covalently coupled to available free carboxyl groups of bovine serum albumin with carbodiimide. The resulting complex was then used for the production of a specific antibody to Act D in two male New Zealand rabbits. Antibody production was of sufficient titer in both rabbits to allow the development of a radioimmunoassay for the free drug which is rapid and sensitive enough to accurately measure 0.1 pmol of Act D. The antibody produced was characterized to be immunoglobulin G by virtue of its ability to bind to Protein A:Sepharose columns. With the use of Act-D analog, actinomine, the antibody was characterized to be specific for the pentapeptide portion of the molecule. Pharmacokinetic analysis of serial serum samples obtained from a patient who received the drug iv revealed a biphasic response with an alpha-serum half-life of 1.78 min and a beta serum half-life of 34 min. An iv injection of Act D into a dog and assay of serum concentration revealed a similar biphasic response with an alpha serum half-life of 0.78 min and a beta-serum half-life of 208 min. (Author abstract) (14 Refs)

6. CHEMICAL SYNTHESIS OF ALPHA-L-FUCOPYRANOSYLCERAMIDE AND ITS ANALOGUES AND PREPARATION OF ANTIBODIES DIRECTED TO THIS GLYCOLIPID.

Yoshino T, Watanabe K, Hakomori S

Dept. Chemistry, International Christian Univ., Mitaka, Tokyo, Japan

Biochemistry; 21(5):928-934 1982

A novel glycolipid, alpha-L-fucopyranosylceramide, was previously isolated and characterized from metastatic human adenocarcinoma. For further investigation of the pathobiological significance of this glycolipid with its specific antibodies, the antigen glycolipid alpha-L-fucopyranosylceramide was chemically synthesized by Konigs-Knorr-type condensation of 2,3,4-tri-O-benzyl-alpha-L-fucopyranosyl bromide and a ceramide, followed by removal of benzyl groups by catalytic hydrogenation. Alpha-L-Fucopyranosyl-N-palmitoylethanolamine and 2,3,4-tri-O-benzyl-alpha-L-fucopyranosylsphingosine were also synthesized. The antibodies prepared against a synthetic alpha-L-fucopyranosylceramide included in liposome reacted very well with the synthetic as well as the natural alpha-L-fucopyranosylceramide isolated from human adenocarcinoma, but the kinetics of the complement-dependent liposome lysis and the complement fixation pattern with the synthetic fucosylceramide were significantly different from those with the natural fucosylceramide. The natural fucosylceramide showed a much weaker immunogenicity than the synthetic fucosylceramide. The remarkable difference in liposome lysis, complement fixation, and immunogenicity between the synthetic and the natural fucosylceramide must be due to the difference in ceramide structures. The results indicate that the strength of antigenicity and immunogenicity of glycolipids may greatly depend on ceramide structure, whereas the specificity is solely determined by the sugar moiety. The anti-alpha-L-fucosylceramide antibodies display cross-reactivity with galactosylceramide, ceramide, and liposome alone that was eliminated by absorption with galactosylceramide liposomes. (Author abstract) (14 Refs)

7. MONOCLONAL ANTIBODIES AGAINST POLYOMA VIRUS TUMOR ANTIGENS.

Dilworth SM, Griffin BE

Imperial Cancer Res. Fund, Lincoln's Inn Fields, P. O. Box 123, London WC2A 3PX, England

Proc Natl Acad Sci USA; 79(4,part1):1059-1063 1982

A method is described for the production of hybridoma cell lines secreting antibodies directed against the polyoma virus tumor antigens (T-Ags). Ten cloned lines have been established by this procedure and designated alphaPy Cl and C4, with activities against all three T-Ags; alphaPy LT1,-4, and-7, with activities against large T-Ag only; and alphaPy MT5,-7,-10, 13, and-16, with activities against middle T-Ag only. Some of the antibodies appear to react also with specific cellular proteins. Data from studies on alphaPy MT7 point to the possible existence of more than one antigenic form of the viral middle T-Ag and, similarly, from studies on alphaPy LT7, to more than one form of large T-Ag. The approx positions on the polyoma virus genome of the sequences encoding antigenic determinants have been mapped by using defined polyoma virus deletion mutants. The availability of these monoclonal antibodies allows the isolation of large amounts of viral T-Ags. (Author abstract) (30 Refs)

8. PHORBOL ESTER-INDUCED DIFFERENTIATION OF A NON-T, NON-B LEUKEMIC CELL LINE: MODEL FOR HUMAN LYMPHOID PROGENITOR CELL DEVELOPMENT.

LeBien TW, Bollum FJ, Yasmineh WG, Kersey JH
Dept. Lab. Medicine and Pathology, Univ. Minnesota, Box 609 Mayo, Minneapolis, MN, 55455
J Immunol; 128(3):1316-1320 1982

The phorbol ester 12-O-tetradecanoylphorbol-13-acetate (TPA) was tested for its ability to induce phenotypic changes in the human non-T, non-B ALL cell line REH. Cells were cultured with nanogram concentrations of TPA for up to 48 hr, and were analyzed by indirect immunofluorescence with a panel of monoclonal antibodies and an antibody to the enzyme terminal deoxynucleotidyl transferase (TdT). TPA induced REH cells to express the leukemia-associated antigen, p24 (detected with monoclonal antibody BA-2; p24/BA-2) by 8 hr of culture, with induction complete by 24 hr. TPA-treated cells also underwent a concomitant decrease in the expression of TdT when analyzed enzymatically or by immunofluorescence. Analysis of TPA-treated cells with monoclonal antibodies BA-1 (detecting a B cell-associated antigen), 7.2 (detecting a monomorphic HLA-DR antigen), or OKT11 (detecting a structure closely associated with the E receptor) showed no change compared to controls. In addition there was no detectable cytoplasmic immunoglobulin in control or TPA-treated cells. These results show clearly that TPA is capable of inducing phenotypic changes in REH cells. Such changes may reflect the differentiation-linked expression of antigens present in normal bone marrow lymphoid progenitor cells. (Author abstract) (41 Refs)

9. HIGH AND LOW FC IGG-RECEPTOR EXPRESSION IN HUMAN CHRONIC GRANULOCYTIC LEUKAEMIA CELLS.

Harlozinska A, Potomski J, Lawinska B, Noworolska A, Richter R
Dept. Pathological Anatomy, Sch. Medicine, ul. Marcinkowskiego 1, 50-368 Wroclaw, Poland
Br J Cancer; 45(2):194-200 1982

Discontinuous density-gradient centrifugation was used to separate chronic granulocytic leukemia (CGL) cells in the chronic phase and blast crisis (BC) into fractions containing granulocytes in individual stages of maturation. The occurrence of the Fc IgG (FcR) and complement-component receptors (CR1 and CR2) in each fraction was estimated. It was established that, with increasing yields of mature granulocytes, the proportion of cells bearing Fc and C3 receptors increased. The most important finding was that the high- and low-receptor categories of CGL cells in chronic phase depended on the percentage of FcR+ cells. In the high-receptor CGL group, in addition to FcR, the proportion of CR1+ and CR2+ cells was also greater than in the low-receptor CGL group. Some differences in clinical course of both immunological CGL groups were observed. (Author abstract) (12 Refs)

10. INDUCTION OF PROLIFERATION AND IG PRODUCTION IN HUMAN B LEUKEMIC CELLS BY ANTI-IMMUNOGLOBULINS AND T CELL FACTORS.

Yoshizaki K, Nakagawa T, Kaieda T, Muraguchi A, Yamamura Y, Kishimoto T
Third Dept. Medicine, Osaka Univ. Medical Sch., Fukushima-ku, Osaka 553, Japan
J Immunol; 128(3):1296-1301 1982

The proliferation and differentiation of human leukemic B cells (B-CLL cells) with anti-Ig and T cell-derived helper factors are described. Stimulation of B-CLL cells with anti-Ig and T helper factors could induce proliferation as well as differentiation into IgM- and IgG-producing cells. Neither anti-Ig nor T helper factors alone could induce any proliferation and/or differentiation of B-CLL cells. Not only whole molecules of anti-Ig but also F(ab')2 fragments could induce proliferation and differentiation of B-CLL cells in the presence of T helper factors, but monovalent Fab' fragments were not effective. Induction of both IgM and IgG with the same idiotype was confirmed by immunofluorescent and SDS-PAGE analysis. By employing an IL 2-dependent cytotoxic T cell line and a TRF-responsive B cell line, T cell factors were separated into a fraction with IL 2 activity but no TRF activity and a fraction with TRF activity but no IL 2 activity by chromatofocusing. Anti-Ig and IL 2 fraction could induce proliferation of B-CLL cells, but TRF fraction was not effective for the induction of proliferation in anti-Ig-stimulated cells. For IgM and IgG production, anti-Ig and both IL 2 and TRF fractions were required. Depletion of IL 2 fraction in the first 2 days' culture inhibited Ig production, whereas the absence of TRF fraction in the firs t 2 days did not show any inhibitory effect on Ig production. (Author abstract) (26 Refs)

11. IMMUNOPEROXIDASE STUDY OF THE SECRETORY IMMUNOGLOBULIN SYSTEM IN COLONIC NEOPLASIA.

Isaacson P
Dept. Pathology, General Hosp., Level E. South Laboratory Block, Southampton SO9 4XY, England
J Clin Pathol; 35(1):14-25 1982

The relation of the secretory immunoglobulin system in the colon to colorectal cancer and dysplasia has been examined by staining routine formalin-fixed, paraffin-embedded sections from cases of carcinoma, adenoma and ulcerative colitis for secretory component (SC), IgA and J chain. In carcinomas there was a close relation between SC synthesis and differentiation and a similar relation was apparent between SC synthesis and degrees of dysplasia in adenomas. In both morphological and functional (SC synthesis) terms degree of dysplasia in adenomas resembled degrees of differentiation in carcinomas suggesting that the essential 'switch' in the progression towards neoplasia may occur at the level of the adenoma and that invasive malignancy can arise from dysplastic mucosa of varying severity. Actively regenerating mucosa in ulcerative colitis (UC) showed intense staining for SC as opposed to foci of precancerous dysplasia where, with one exception, staining was markedly reduced or absent, suggesting staining for SC could be useful in identifying foci of precancerous dysplasia in UC. In the absence of severe chronic inflammation, as in UC, the number of IgA-containing plasma cells was closely related to SC staining of neoplastic mucosa suggesting that SC may be important in the mechanism by which IgA lymphocytes home to the lamina propria of the colon. (Author abstract) (13 Refs)

12. PRODUCTION OF MONOCLONAL ANTIBODY ALPHAPRO3 RECOGNIZING A HUMAN PROSTATIC CARCINOMA ANTIGEN.

Ware JL, Paulson DF, Parks SF, Webb KS
Dept. Surgery, Div. Urology, Duke Univ. Medical Center, Durham, NC, 27710
Cancer Res; 42(4):1215-1222 1982

The monoclonal antibody alphaPro3 recognizes an antigen concentrated in human primary prostatic carcinoma tissue removed surgically. Although the antigen was detectable in extracts of human normal and malignant nonprostatic tissue, as well as in benign prostate tissue, quantitative absorption analysis revealed a substantially greater quantity of the antigen in malignant prostate tissue. The antigen recognized by alphaPro3 in primary prostatic carcinoma has an apparent nonreduced molecular weight of 175,000 and an apparent subunit molecular weight of 54,000. This antigen, p54, appears to be present on the surface of cultured prostatic tumor cells of the PC-3 cell line, but its location in vivo has been defined. Successful competition between alphaPro3 and prostatic carcinoma patient serum immunoglobulin for a Mr 54,000 antigen (reduced molecular weight) present in prostatic carcinoma tissue extract suggests that p54 may play a significant role in the immunobiology of prostatic carcinoma. AlphaPro3 has potential as a sensitive probe for an antigen relevant to human tumor biology. (Author abstract) (46 Refs)

TUMOR ANTIBODIES ASSOCIATED WITH VIRUSES

13. MONOCLONAL ANTIBODIES TO XENOTROPIC AND MCF MURINE LEUKEMIA VIRUSES DERIVED DURING THE GRAFT-VERSUS-HOST REACTION.

Portis JL, McAtee FJ, Cloyd MW

Dept. Health and Human Services, Public Health Service, NIH, Natl. Inst. Allergy and Infectious Diseases, Rocky Mountain Lab., Hamilton, MT, 59840

Virology; 118(1):181-190 1982

The humoral immune response during adult graft-vs-host reaction (GVHR) was assessed by the recovery of antibody-forming host spleen cells using cell fusion techniques. Two parent - F1 strain combinations were studied, (B6 x D2)F1 and (NFS x AKR)F1 injected with the respective parental spleen cells. Hybridomas derived from recipient spleens were found to produce antibody with predominant specificity for murine leukemia virus (MuLV) envelope (env) polypeptides. The recovery of anti-MuLV monoclonal antibodies was dependent on the donor strain. Thus, D2-(B6 x D2)F1 and AKR - (NFS x AKR) resulted in a high incidence of anti-MuLV antibody production among the primary fusion products whereas no anti-MuLV hybridomas were recovered when B6 or NFS, respectively, were used as donors. Hybridomas derived from D2-(B6 x D2)F1 produced anti-MuLV antibodies of two general specificities: (1) broadly reactive, detecting determinants expressed by ecotropic and xenotropic MuLV, and (2) xenotropic MuLV specific. The latter group included antibodies reacting with all xenotropic MuLV and antibodies with xenotropic MuLV strain specificity. Xenotropic MuLV-specific determinants were expressed by gp70, p15(E), and the gp70-p15(E) complex (gp90). This is, to our knowledge, the first report of monoclonal antibodies specific for xenotropic MuLV. In contrast, hybridomas derived from AKR - (NFS x AKR) produced antibodies which reacted predominantly with unique determinants of a subgroup of MCF viruses. These results suggested that the anti-MuLV antibody repertoire expressed during GVHR is influenced by the endogenous MuLV of the respective mouse strain combination. (Author abstract) (25 Refs)

14. AN IGM-PRODUCING B LYMPHOBLASTOID CELL LINE ESTABLISHED FROM LYMPHOMAS INDUCED BY A NON-DEFECTIVE RETICULOENDOTHELIOSIS VIRUS.

Nazerian K, Witter RL, Crittenden LB, Noori-Dalloii MR, Kung HJ

Regional Poultry Res. Lab., U.S. Dept. Agriculture, 3606, East Mount Hope Road, East Lansing, MI, 48823

J Gen Virol; 58(part2):351-360 1982

Chick syncytial virus (CSV), a strain of avian reticuloendotheliosis virus (REV) causes lymphoid tumors in chickens after a prolonged incubation period. A number of CSV-induced tumors were examined for cell surface antigen and were found to be of the B cell type and to produce immunoglobulin. Attempts were made to grow in vitro cell lines from CSV-induced tumors and a lymphoblastoid cell line was established from a liver tumor of a chicken that was inoculated with CSV via the yolk sac in embryo. The donor chicken was viremic at the time the tumor was removed. The cell line is designated RECC-RP13, it produces non-defective REV, is a B cell type and it produces IgM. It is free from infection with endogenous and exogenous avian leukosis virus (ALV) and has an increased number of chromosomes. Sequences specific to REV were detected in at least four sites in cellular DNA from RECC-RP13. Sequences specific to ALV DNA, beyond that normally found in 15I5 x 71 cells, were not found in DNA from this cell line. (Author abstract) (31 Refs)

15. DIAGNOSIS OF BOVINE LEUKOSIS VIRUS INFECTION BY SOLID PHASE RADIOIMMUNOASSAY FOR VIRUS ANTIBODY.

Zajac V, Altaner C

Cancer Res. Inst., Slovak Acad. Sciences, 812 32 Bratislava, Czechoslovakia

Neoplasma; 28(6):661-668 1981

Solid phase radioimmunoassay for detection of anti-BLV antibodies in sera of infected animals is described. Viral antigens bound to the surface of polystyrene are able to selectively adsorb the antibodies from serum. Detection of bound antibodies quantitatively was done by 125I-labeled protein A from Staphylococcus aureus. Technical details of the assay are reported. The assay could be used as a competitive one as well. Two different methods for detection of anti-BLV antibodies were compared with solid phase RIA. The solid phase RIA is highly sensitive, specific and available for large-scale examination. The assay is recommended for early diagnosis of bovine leukosis. (Author abstract) (18 Refs)

16. SPECTRUM OF TUMORIGENIC PHENOTYPES AMONG ADENOVIRUS 2-, ADENOVIRUS 12-, AND SIMIAN VIRUS 40-TRANSFORMED SYRIAN HAMSTER CELLS DEFINED BY HOST CELLULAR IMMUNE-TUMOR CELL INTERACTIONS.

Lewis AM, Cook JL

Natl. Inst. Allergy and Infectious Diseases, NIH, Bethesda, MD, 20205

Cancer Res; 42(3):939-944 1982

The tumor-inducing capacities of adenovirus Type 2-, adenovirus Type 12-, and SV40-transformed LSH hamster embryo cells define a spectrum of four distinct tumorigenic phenotypes: Type I, nononcogenic for newborn hamsters but oncogenic for nude mice; Type II, oncogenic for new born hamsters but non-oncogenic in syngeneic adults; Type III, oncogenic for both newborns and syngeneic adults; and Type IV, almost equally oncogenic for syngeneic and allogeneic adult hamsters. Modulation of the cellular immune response of the recipient hamster by immunosuppression or by alloimmunization alters tumor susceptibility, suggesting that dynamic transformed cell-host cellular immune interactions determine the tumorigenic phenotype of a transformed cell line. There is no correlation between the immunogenicities of the transformed cell lines tested and their tumor-inducing capacities. However, a strong correlation exists between the ability of transformed hamster embryo cells expressing Phenotype IV to produce tumors in allogeneic CB hamsters and their resistance to cytolysis in vitro by activated macrophages. These data suggest that, in addition to transformation, DNA viruses may convey specific tumorigenic phenotypes to the cells that they infect by inducing cellular traits that determine the inherent susceptibility or resistance of a cell to host cell-mediated immune destruction. (Author abstract) (29 Refs)

17. ANTI-TUMOR IMMUNITY IN B-LYMPHOCYTE-DEPRIVED MICE. III. IMMUNITY TO PRIMARY MOLONEY SARCOMA VIRUS-INDUCED TUMORS.

Gordon J, Holden HT, Segal S, Feldman M
Weizman Inst. Science, Rehovot, Israel
Int J Cancer; 29(3):351-357 1982

Tumor induction and immunity to tumors were studied following the injection of Moloney sarcoma virus (MSV) into mice whose B-lymphocyte functions had been suppressed by the chronic administration of anti-IgM antibodies. Two preparations of MSV were used, one which gives rise to tumors which uniformly regress in normal adult mice, and another which elicits progressively growing tumors in the majority of recipients. The tumor incidence, mean tumor size, and tempo of regression were not modified by treatment with anti-IgM. However, whereas tumors induced by the regressor virus were all rejected in 19 NRG-treated and 29 untreated recipients, continued growth was obtained in 2 of 23 B-lymphocyte-deprived mice. Furthermore, in nine additional mice from this group, apparent rejection was followed by tumor recurrence at the site of the initial tumor. Continued growth was accompanied by widespread metastasis. These tumors were freely transplantable to normal syngeneic recipients. Metastasis and transplantability were also detected in 7 of 24 anti-IgM-treated mice given progressor virus, but were not seen in the control animals. Recurrence and metastasis was obtained despite the presence of high levels of specific cytotoxic T lymphocytes in the spleen. It is concluded that B lymphocytes or their products play an essential role in hot protection against MSV-induced tumors. (Author abstract) (29 Refs)

18. COMPLEMENT-FIXING ANTIBODY TO EPSTEIN-BARR VIRUS SOLUBLE ANTIGEN IN POPULATIONS AT HIGH AND LOW RISK FOR NASOPHARYNGEAL CARCINOMA.

Levine PH, Ebbesen P, Connelly RR, Das S, Middleton M, Mestre M
NCI, Landow Bldg., ID-12, Bethesda, MD, 20205
Int J Cancer; 29(3):265-268 1982

Greenland Eskimos comprise an ethnic group with one of the highest recorded incidence rates for nasopharyngeal carcinoma in the world. Sera from 625 Eskimos and 73 Danes (Caucasians) living in Greenland, as well as from 62 Danes living in Denmark, were tested for complement-fixing an tibody to Epstein-Barr virus (EBV) soluble antigen and, from this study group, 129 donors were matched by age and sex for a study comparing antibody to viral capsid antigen, early antigen, and soluble antigen. Both Eskimos and Danes living in Greenland had significantly higher titers of EBV antibodies than Danes living in Denmark, suggesting that environment was more important than genetics or socioeconomic factors in determining the antibody response to EBV. Age and sex were also factors, higher titers occurring in females and young Eskimos. (Author abstract) (21 Refs)

19. GLIOMAS INDUCED IN MAMMALS BY ROUS SARCOMA VIRUS.

Rabotti GF
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Neurochirurgie; 27(5):247-249 1981

Meningeal tumors induced by Rous Sarcoma virus (RSV) have been produced in chickens, rabbits, cats, and dogs. Nonhuman primates have also been used, but the in vivo results following inoculation have been negative. The greatest percentage of positive results has been obtained following intracerebral inoculation in the course of the 24 hr following birth. Tumors have been induced in older animals but the number of positive cases is considerably reduced. Most induced tumors were histological mixed types, but true gliomas have been observed. Infectious doses of RSV induced tumor formation in the chicken which is the natural host of the virus. In mammals oncogenic doses had to be injected to induced tumor formation. Efforts are currently underway to fix antiviral antibodies on the surface of glioma cells in vivo in hamsters, rats, and dogs. Further studies include the in vivo fixation of immune lymphocytes. Nothing is presently known of the immune response in an animal with a primary glioma induced by RSV. (17 Refs) (In FRE)

20. IMMUNOGLOBULIN PROPERTIES OF EPSTEIN-BARR VIRUS TRANSFORMED HUMAN UMBILICAL CORD AND ADULT PERIPHERAL BLOOD LYMPHOCYTES.

Konowalchuk J, Speirs JI, Perelmutter L
Lab. Centre Disease Control, Health Protection Branch, Health and Welfare Canada, Ottawa K1A 0L2, Canada
Cell Immunol; 67(1):190-196 1982

Lymphocytes from umbilical cords and peripheral adult blood were transformed with Epstein-Barr virus. Cultures of these transformed cells were studied for cell-associated and secreted immunoglobulins (Ig) and for their stability after long-term culture. The adult cell lines produced intracellular and extracellular Ig of all five classes but there was a paucity of IgA in cord cell cultures. Cells producing cytoplasmic Ig were at least 10 times more numerous than those secreting Ig. Both cord and adult lines appeared relatively stable after months of culture indicating that both may be useful in the preparation of immunological reagents. (Author abstract) (21 Refs)

21. ANTIVIRAL SPECIFICITIES OF IMMUNOGLOBULINS SECRETED BY HUMAN LYMPHOCYTES IMMORTALIZED IN VITRO WITH EPSTEIN-BARR VIRUS.

Seigneurin JM, Desgranges C, Reneversez JC, Baccard M, Micouin C
Laboratoire de Virologie, Centre Hospitalier Universitaire, Grenoble, France
Ann Virol; 132(3):323-335 1981

Human B lymphocytes from a chronic T-lymphocytic leukemia patient were immortalized through the use of two Epstein-Barr (EBV) strains, both obtained after passage in marmoset lymphocytes, Ma-B95-8 from an infectious mononucleosis patient, and Ma-M81 from lymphocytes invading the tumor of a nasopharyngeal carcinoma patient. Features of the two established cell lines are described especially in relation to polyclonal synthesis of virus specific antibodies. Characteristics of the patient's lymphocytes are described. The two cell lines established were clearly of B-cell origin. Both cell lines contained Epstein-Barr nuclear antigen in 100% of the cells. EBV early antigen was evident in 1.8% of Ma-B95 cells and 3.0% of Ma-M81 cells. EBV viral capsid antigen was found only in 3.0% of Ma-M81 cells. Both lines expressed complement 3 and EBV receptors and surface-bound immunoglobulin. Ultrastructurally, Ma-M81 had the typical features of a lymphoblastoid cell line, while Ma-B95 had features of plasmacytoid cells. Ma-B95 cells secreted a high level of immunoglobulins (32 ug/10(6) cells), including 24 ug IgG, while Ma-M81 cells produced only 3.8 ug. At the time the cell lines were established, the patient possessed antiviral antibodies against several viruses, cytomegalovirus, respiratory syncytial virus, and measles virus, which were found in the immunoglobulin secreted by Ma-B95. The Ma-M81 cell line produced complete EBV virion, while in the Ma-B95 cells the replicative cycle of EBV was blocked at the early antigen stage. (39 Refs)

22. INDUCTION AND INHIBITION OF THE IMMUNE RESPONSE TO TUMORS INDUCED BY SIMIAN VIRUS 40 (SV40).

Blasecki JW
Pharmaceuticals Div., Stine Lab., E.I. du Pont de Nemours and Co., Newark, DE, 19711
The Handbook of Cancer Immunology: Volume 8- Tumor Antigens: Structure and Function. Waters H, ed. New York, STPM Garland Press, 418 pp., 1981.

The growth or rejection of SV40-induced tumors in immunocompetent hosts is determined by a dynamic balance among cellular and humoral responses to the tumor and the effects of products shed from the tumor cells (apparently surface-associated antigens) on this balance. The first step in the immune response to the tumor seems to be the processing of SV40 tumor-specific transplantation antigens (TSTA) by the macrophages (or perhaps natural killer cells) and the presentation of TSTA to the T-lymphocytes. This leads to the appearance of sensitized T-cells having specific cytolytic activity against SV40 tumor cells. Cytotoxic antibodies apparently do not play a significant role in tumor rejection. The induction of immunity to SV40 TSTA is not the only aspect of the host-tumor interaction, but inhibition of the antitumor immune response is apparently critical to favoring tumor growth. SV40 TSTA seems to play an important role in abrogating specific cellular immunity to SV40 tumors in vivo. Antibody or antigen-antibody complexes seem to block cellular immunity to SV40 tumors at the cellular level. Progressive tumor growth apparently causes a specific or nonspecific suppression of helper T-cell activity. The suppression of antibody synthesis in tumor-bearing hosts may be involved in preventing antibody-mediated sequestration of tumor-associated antigens, thus enhancing tumor growth. Soluble blocking factors and suppressor cells also seem to be involved in regulating host immune responses to SV40-induced tumors. (217 Refs)

23. SHORT COMMUNICATIONS. THE INCREASED NATURAL KILLER SENSITIVITY OF EPSTEIN-BARR VIRUS (EBV)-SUPERINFECTED RAJI CELLS IS NOT DUE TO THE RECOGNITION OF SEROLOGICALLY DETERMINED EBV ANTIGENS BY THE EFFECTORS.

Patarroyo M, Klein E, Klein G
Dept. Tumor Biology, Karolinska Inst., S-104 01 Stockholm, Sweden
Cell Immunol; 67(1):152-159 1982

The NK sensitivity of Raji cells was elevated after superinfection with the P3HR-1 strain of Epstein-Barr virus (EBV). The superinfected cells reacted with EBV antibody-positive sera and this was detectable by ADCC. F(ab')2 fragments from the antibody-positive sera blocked the ADCC reaction but did not affect attachment of lymphocytes and natural killing. This indicates that the EBV-determined membrane antigens that serve as targets for the reactivity with the sera are not responsible for the increased NK sensitivity. (Author abstract) (19 Refs)

ANTITUMOR ACTIVITY AND IMMUNOTHERAPY

24. NEOPLASTIC B CELLS AS TARGETS FOR ANTIBODY-RICIN A CHAIN IMMUNOTOXINS.

Vitetta ES, Krolick KA, Uhr JW
Dept. Microbiology, Univ. Texas Health Science Center at Dallas, Dallas, TX, 75235
Immunol Rev; 62:159-183 1982

Studies assessing the capacity of antibody-ricin A chain conjugates (immunotoxins) to selectively kill tumor cells from the murine B cell tumor, BCL1, are reviewed. The extent to which BCL1 cells could be selectively killed in vitro was determined. The ability of BCL1 cells present in tumor-infiltrated bone marrow to kill in vitro without harming hematopoietic stem cells was examined. Experiments designed to determine the effectiveness of the anti-immunoglobulin (Ig) immunotoxins in vivo using mice bearing advanced BCL1 tumors are described. The BCL1 tumor model, preparation of antibodies, preparation of anti-Ig immunotoxins, and adoptive transfer of BCL1 cells treated with antibody A-chain immunotoxin are discussed. The implications for bone marrow transplantation in the treatment of malignancy are considered in rel ation to the elimination of BCL1 tumor cells from bone marrow. (56 Refs)

25. THE PREPARATION AND CYTOTOXIC PROPERTIES OF ANTIBODY-TOXIN CONJUGATES.

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Immunol Rev; 62:119-158 1982

Preparation and cytotoxic properties of toxin-antibody conjugates, particularly the ways in which different types of linkage used in constructing the conjugate influence its biology, are reviewed. Ways in which the non-specific cytotoxicity of conjugates with intact toxins can be reduced are described. Two approaches for the synthesis of selective cytotoxic agents from antibodies and toxins are the linkage of intact toxin to a bivalent antibody and the linkage of the isolated A-chain derived from a toxin directly to the antibody molecule. Naturally-occuring toxin A-chains, which are virtually free from toxicity to intact cells, may be used. The cytotoxic and anti-tumor activities are described for a conjugate containing one such inhibitor, gelonin, from Gelonium multiflorum. Preparation of conjugates using chlorambucil derivatives, N-succinimidyl-3(2-pyridyldithio)propionate, and haloacetyl derivates, purification procedures, and calculation of the composition of the conjugates are discussed. Cytotoxic properties of antibody-toxin conjugates are considered in relation to conjugates with intact toxins (diphtheria toxin, abrin, ricin), abrogation of the non-specific antibody-toxin conjugates (competitive antagonism of the non-specific toxicity of antibody-abrin and antibody-ricin conjugates with galactose or lactose, conjugates with abrin modified chemically to block its galactose-binding site), and conjugates with diphtheria toxin or ricin A-chains or gelonin. Cell-type-specific cytotoxicity may be achieved using conjugates of antibodies and intact toxins or their A-fragments. (76 Refs)

26. ANTIBODY MEDIATED DELIVERY OF TOXIC MOLECULES TO ANTIGEN BEARING TARGET CELLS.

Raso V
Sidney Farber Cancer Inst., 44 Binney St., Boston, MA, 02115
Immunol Rev; 62:93-117 1982

The ability of hybrid antibodies with dual specificity to deliver toxic agents to immunoglobulin (Ig)-bearing target cells is reviewed. Progress on both the Ig and CALLA (conjugates which are selectively cytotoxic for human cells bearing the acute lymphoblastic leukemia antigen) are discussed. Topics discussed include hybrid antibodies with simultaneous cell surface and toxic agent binding activity (anti-neocarzinostatin, anti-human IgG hybrids and anti-ricin A chain/anti-human IgG hybrids) and selectively cytotoxic antibody-ricin A chain conjugates (human Ig directed antigen binding fragment [F(ab')]-A chain conjugate, monoclonal human kappa-chain specific F(ab')2-A chain conjugate, and monoclonal CALLA-specific F(ab')-A chain conjugates). Hybrid-mediated enhancement of toxicity has been achieved using neocarzinostatin, whole ricin, and free ricin A chain. (43 Refs)

27. MONOCLONAL ANTIBODY-RICIN OR RICIN A CHAIN HYBRIDS: KINETIC ANALYSIS OF CELL KILLING FOR TUMOR THERAPY.

Neville DM, Youle RJ
Lab. Neurochemistry, Section on Biophysical Chemistry, Natl. Inst. Mental Health, Bethesda, MD, 20205
Immunol Rev; 62:75-91 1982

Effects of three different types of ricin hybrids (antibody thioether linked to intact ricin, antibody disulfide linked to the ricin A chain, and antibody-S-S-A chain to which the ricin B chain is added as a separate entity) conjugated with monoclonal antibody having affinity for the murine thymic adult differentiation antigen Thy 1 on targeted cells are reviewed in relation to tumor cytotoxicity. Entry mechanisms and data regarding parent toxins are considered. (30 Refs)

28. NATURAL CYTOTOXICITY AND ANTIBODY-DEPENDENT CYTOTOXICITY IN SOLID TUMOR CANCER PATIENTS: REGULATION BY ADHERENT CELLS.

DeBoer KP, Braun DP, Harris JE
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Clin Immunol Immunopathol; 23(1):133-144 1982

Natural cytotoxicity (NK) and antibody-dependent cellular cytotoxicity (ADCC) were measured in peripheral blood mononuclear cells (PBMC) from 30 normal subjects and from 60 untreated patients with solid tumors at various stages of disease. NK, but not ADCC, activity of PBMC from patients with disseminated disease was significantly lower than NK activity of either normal donors or patients with localized disease. This decreased NK activity was not related to decreased numbers of T cells or target-binding cells or to immune complex levels in patient sera. Glass-adherent cell depletion augmented decreased NK levels significantly to normal levels of function. Addition of indomethacin did not alter NK activity in any of the patients studied. We conclude that decreased NK activity in PBMC from cancer patients with disseminated disease is due to a suppression which may be mediated by glass-adherent cells. This is not dependent on a prostaglandin-mediated mechanism of suppression. (Author abstract) (28 Refs)

29. COMPARISON OF CURRENTLY AVAILABLE MONOCLONAL ANTIBODIES WITH CONVENTIONAL MARKERS FOR PHENOTYPING OF ONE HUNDRED ACUTE LEUKEMIAS.

Thiel E, Kummer U, Rodt H, Stunkel K, Munker R, Majdic O, Knapp W, Thierfelder S
Abteilung Immunologie, Institut fur Hamatologie, GSF, Landwehrstr. 61, D-8000 Munchen 2, W. Germany
Blut; 44(2):95-100 1982

Monoclonal antibodies (mAbs) were compared with conventional antisera for phenotyping acute leukemias. One hundred frozen bone marrow samples were tested. All had been obtained at the time of diagnosis from children with acute leukemia. Samples were typed by reaction with conventional antibody p reparations including sheep RBC receptor, surface immunoglobulins, rabbit anti-common acute lymphoid leukemia (anti-cALL) serum, rabbit anti-thymocyte/T cell serum, and rabbit anti-granulocyte serum against myelomonocytic antigens. Fifteen mAbs were tested. VIL-A1 mAbs, directed against the cALL antigen, reacted like rabbit polyclonal antibody in 95/100 serum samples. Other mAbs reacted with considerable heterogeneity. Those mAbs directed against T-cell antigens were capable of classifying subgroups of leukemias according to the degree of T-cell maturation. Detection of OKM1 antigen was indicated as a possible means of diagnosing acute myelomonocytic leukemia. All 'pan-T' mAbs failed to detect some individual samples tested, although general reactive patterns were strong. Diagnostic use of mAbs will require selection of mAbs that react with essential epitopes. (15 Refs)

30. USE OF ANTI-T-CELL MONOCLONAL ANTIBODY OKT3 TO PREVENT ACUTE GRAFT-VERSUS-HOST DISEASE IN ALLOGENEIC BONE-MARROW TRANSPLANTATION FOR ACUTE LEUKAEMIA.

Prentice HG, Janossy G, Skeggs D, Blacklock HA, Bradstock KF, Goldstein G, Hoffbrand AV
Academic Dept. Haematology, Royal Free Hosp. Sch. Medicine, London, England
Lancet; 1(8274):700-703 1982

Seventeen patients who received allogeneic bone-marrow transplants from matched or slightly mismatched (in 4 patients) siblings were observed for at least 60 days or until acute graft-vs-host disease (GvHD) developed. All donor marrows after preliminary manipulation were incubated with 1 mg of the murine monoclonal antibody OKT3 before infusion in an attempt to deplete them of immunocompetent T lymphocytes (opsonization). In 3 of the 17 patients acute GvHD of Grade II or greater developed. Two of these patients died, but they had disseminated cytomegalovirus infection as well as GvHD. Eleven patients showed no evidence of acute GvHD, and 4 had transient limited skin rashes (Grade I GvHD). Opsonization of T Lymphocytes has reduced the incidence of severe acute GvHD in this unit from 79% in an earlier group of 14 patients to 18% when added to prophylactic methotrexate. (Author abstract) (33 Refs)

31. MONOCLONAL ANTIBODIES THAT INHIBIT ENZYME ACTIVITY OF 3-METHYLCHOLANTHRENE-INDUCED CYTOCHROME P-450.

Park SS, Fujino T, West D, Guengerich FP, Gelboin HV
(c/o Gelboin) Lab. Molecular Carcinogenesis, NCI, NIH, Bethesda, MD, 20205
Cancer Res; 42(5):1798-1808 1982

Somatic cell hybrids were made between mouse myeloma cells and spleen cells derived from BALB/c mice immunized with liver microsomal cytochrome P-450 purified from rats treated with 3-methylcholanthrene (MC-P-450). Thirty-seven independent hybrid clones among 66 tested produced monoclonal antibodies to the MC-P-450 as measured by radioimmunoassay. More than 10 of the monoclonal antibodies formed were positive for MC-P-450 with respect to protein binding measured by radioimmunoassay, precipitation of the enzyme caused by antibody binding and enzyme aggregation, and inhibition of enzymatic activity. Analysis by gel electrophoresis indicated that a single microsomal protein band interacted with the antibody and that this band comigrated with MC-P-450. These monoclonal antibodies interacted with the major form of cytochrome P-450 from beta-naphthoflavone-induced rats as well as with MC-P-450 but did not bind, precipitate, or inhibit the activity of the major form of cytochrome P-450 from phenobarbital-treated rats. The monoclonal antibodies inhibited 7-ethoxycoumarin deethylase and benzo(a)pyrene hydroxylation activity of the purified MC-P-450 with varying degrees. Analysis of benzo(a)pyrene metabolism indicated that the monoclonal antibodies inhibited the enzyme activity of the purified MC-P-450 at all of the positions at which oxidation occurs. Analysis of antibody inhibition of benzo(a)pyrene metabolism by microsomes from 3-methylcholanthrene-treated rats showed an inhibition of phenol and diol formation that ranged from 46 to 72%. 1,6-Quinone production was not affected, which suggests that this metabolite was formed by another cytochrome P-450 isozyme or nonenzymatically. The purity, specificity, and potential immortality of their hybridoma cell source will make the monoclonal antibodies extraordinarily useful for the study of substrate and inducer specificity and in the identification and quantitative assay of multiple forms of the cytochrome P-450 and the determination of their content and function in different tissues, species and individuals. (43 Refs)

32. MONOCLONAL ANTIBODY TO LYT 2 ANTIGEN BLOCKS H-2I- AND H-2K-SPECIFIC MOUSE CYTOTOXIC T CELLS.

Miller RA, Stutman O
Memorial Sloan Kettering Cancer Center, New York, NY, 10021
Nature; 296(5852):76-78 1982

Inhibition of mouse cytotoxic lymphocytes (CTL) by monoclonal antibody against Lyt 2 antigen was studied using a 5-day in vitro sensitization culture and 4-hr 51Cr-release assay for cytotoxicity. CTL effectors specific for the I-region of the major histocompatibility (MHC) complex were generated by reciprocal in vitro sensitizations between mouse strains B10.AQR and B10.T(6R), which are congeneic-resistant, and which differ only in the I-region. B10.A stimulators differing only in the K-region served as positive controls. After 5 days of sensitization, cytotoxicity assays were conducted with rat monoclonal antibody to Lyt 2 or with control serum. Anti-Lyt 2 inhibited cytolysis by I-specific and K-specific CTL to the same extent. Inhibition did not require the presence of Lyt 2 antigen on the target cells. CTL cytotoxicity was not inhibited by normal nude mouse serum or by serum from nude mice bearing a hybridoma producing antibody against Lyt 1. Control experiments showed that inhibition was dependent on anti-Lyt 2 and not on other unidentified factors. Results indicate that Lyt 2-bearing molecules probably have equivalent roles regardless of the genetic region controlling the target cells recognized by the CTL, and that I-specific CTL must be Lyt 2-positive. (26 Refs)

33. UNIQUE GLYCOPROTEIN-PROTEOGLYCAN COMPLEX DEFINED BY MONOCLONAL ANTIBODY ON HUMAN MELANOMA CELLS.

Bumol TF, Reisfeld RA
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Proc Natl Acad Sci USA; 79(4,part1):1245-1249 1982

A monoclonal antibody, 9.2.27, with a high specificity for human melanoma cell surfaces has been utilized for biosynthetic studies in M21 human melanoma cells to define a unique antigenic complex consisting of a 250-kilodalton N-linked glycoprotein and a high mol wt proteoglycan component larger than 400 kilodaltons. The 250-kilodalton glycoprotein has endoglycosidase H-sensitive precursors and shows a lower apparent mol wt after treatment with neuraminidase. The biosynthesis of the proteoglycan component is inhibited by exposure of M21 cells to the monovalent ionophore monensin; this component can be labeled biosynthetically with 35SO4, is sensitive to beta-elimination in dilute base, and is degraded by both chondroitinase AC and ABC lyases, suggesting that it is a chondroitin sulfate proteoglycan. These data demonstrate that the antigenic determinant recognized by monoclonal antibody 9.2.27 is located on a glycoprotein-proteoglycan complex which may have unique implications for the interaction of glycoconjugates at the human melanoma tumor cell surface. (Author abstract) (29 Refs)

34. MONOCLONAL ANTIBODY TO TRANSFERRIN RECEPTOR BLOCKS TRANSFERRIN BINDING AND INHIBITS HUMAN TUMOR CELL GROWTH IN VITRO.

Trowbridge IS, Lopez F
Dept. Cancer Biology, Salk Inst. Biological Studies, P. O. Box 85800, San Diego, CA, 92138
Proc Natl Acad Sci USA; 79(4,part1):1175-1179 1982

A murine hybridoma has been obtained that produces a monoclonal antibody against the human transferrin receptor. In contrast to previously characterized monoclonal antibodies that recognize the transferrin receptor, this antibody, designated 42/6, blocks the binding of transferrin to its receptor and inhibits the growth of the human T leukemic cell line, CCRF-CEM, in vitro. Inhibition of cell growth was dose dependent, and as little as 2.5 ug of purified antibody per ml had a detectable effect, even though transferrin was present in the tissue culture medium in large molar excess. Cells grown in the presence of antibody for 7 days accumulated in S phase of the cell cycle. The addition of iron to antibody-treated cultures in the form of ferric complexes or ferrous sulfate did not overcome the growth inhibitory effects of the anti-transferrin-receptor antibodies. This result suggests that either transferrin is the only means by which CCRF-CEM leukemic cells can be provided with sufficient iron in vitro or that other factors in addition to iron starvation are involved in the antibody-mediated growth inhibition. The inhibition of cell growth by 42/6 monoclonal antibody suggests that monoclonal antibodies against proliferation-associated cell surface antigens, such as the transferrin receptor, may be useful pharmacological reagents to modify cell growth in vitro. (Author abstract) (46 Refs)

35. IN VITRO AND IN VIVO EFFICACY OF CONJUGATES OF DAUNOMYCIN WITH ANTI-TUMOR ANTIBODIES.

Arnon R, Sela M
Dept. Chemical Immunology, Weizmann Inst. Science, Rehovot 76100, Israel
Immunol Rev; 62:5-27 1982

Studies in vitro and in vivo on daunomycin (DN) conjugates with antibodies to several mouse and rat tumor-selective antigens using both conventional and monoclonal antibodies are summarized. Topics discussed in relation to DNA-antibody conjugates include conjugation (direct binding procedure), linking of DNA via dextran bridge, pharmacological activity of the protein-bound drug, and antibody activity of the conjugates. Other topics discussed include conjugates with antigen binding fragment dimers, in vitro efficacy of conjugates, mode of action of the conjugates (in vitro uptake of DNA conjugates, 'homing' of anti-tumor antibodies and conjugates), in vivo efficacy of the conjugates on murine experimental tumors, and efficacy of conjugates on rat hepatoma. Antibodies may serve as carriers for anti-cancer drugs to tumor cells. (43 Refs)

36. THE NATURE OF TROPHOBLASTIC DISEASE INITIATED BY TRANSPLANTATION INTO IMMUNOSUPPRESSED ANIMALS.

Kato M, Tanaka K, Takeuchi S
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Am J Obstet Gynecol; 142(5):497-505 1982

To elucidate the nature of trophoblastic disease, trophoblastic tissue was transplanted into nu/nu mice and immunosuppressed Syrian hamsters. All tissue was successfully transplanted, with no tumorigenicity shown in either the 21 cases of hydatidiform mole (HM) or the 10 cases of invasive mole (IM). However, in seven of the nine cases of choriocarcinoma (CC), tumorigenicity was demonstrated by successful serial transplantation. Thus, the conclusion was that CC was clearly a malignant neoplasm, whereas IM and HM should be considered to be benign disease because of their cellular behavior, which was clearly distinct from that of CC in this series. (Author abstract) (14 Refs)

37. ENDOTHELIAL CELL PROLIFERATION AS A NOVEL APPROACH TO TARGETING TUMOUR THERAPY.

Denekamp J
Gray Lab., Cancer Res. Campaign, Mount Vernon Hosp., Northwood, Middlesex HA6 2RN, England
Br J Cancer; 45(1):136-139 1982

The tremendous proliferative differential in vascular endothelia of tumors and of normal tissues has potential use in tumor therapy. Conjugation of an S-phase-specific chemotherapeutic agent with an endothelial-cell-specific antibody to cause a large degree of cell killing in tumor capillaries without damaging normal tissue vessels should be possible. Such therapy would be used in combination with radiotherapy and/or chemotherapy. (14 Refs)

38. PHENOTYPE CHARACTERIZATION OF CHRONIC LYMPHOCYTIC LEUKEMIA WITH MONOCLONAL ANTIBODIES AND SURFACE RECEPTORS.

Estevez ME, Sen L, Diez RA, Bellouard A, Santos I
Departamento de Microbiologia, Instituto de Investigaciones, Hematologicas Academia Nacional de Medicina, Buenos Aires, Argentina
Medicina (B Aires); 41(Suppl):123-130 1981

Different immunologic and enzymatic techniques as well as monoclonal antibodies (MA) were used in 33 patients (21 men, 12 women; 42-84 yr old) with chronic lymphocytic leukemia. Analyses were performed when WBC was greater than 10,000/mm square. T cell markers were determined with sheep red blood cell rosette test (E4 and E37). B cell markers were determined using mouse red blood cell rosette formation test (ER). C3 serum complement was determined by erythrocyte antibody complement (EAC) rosette test. Cell surface (sIg) and cytoplasmic (cIg) immunoglobulins were determined by immunofluorescence. Surface antigens T1, T3, T4, T6, T8, T9, T10, T11a, Ia1, and M1 were evaluated with MA of OK series. All the patients had phenotype B and were divided into four groups (early immature, immature, mature, and very mature). EAC was present in all the patients, and only 1/3 had ER values greater than 20%. Range of values was 0-37% for E4, 0-27% for E37, 22-94% for EAC, and 0-82% for ER. Results of monoclonal antibodies were positive in 11/12 patients for Ia1, in 7/12 for T1, and in 2/12 for T10, all the others were negative. (16 Refs) (In SPA)

39. A SINGLE MONOCLONAL ANTI-IA ANTIBODY INHIBITS ANTIGEN-SPECIFIC T CELL PROLIFERATION CONTROLLED BY DISTINCT IR GENES MAPPING IN DIFFERENT H-2 I SUBREGIONS.

Germain RN, Bhattacharya A, Dorf ME, Springer TA
Dept. Pathology, Harvard Medical Sch., Boston, MA, 02115
J Immunol; 128(3):1409-1413 1982

A xenogeneic rat anti-mouse Ia monoclonal antibody, M5/114 (gamma2b,kappa) was studied for its effects in vitro on T cell proliferative responses. Strain distribution studies revealed that M5/114 could inhibit I-A subregion-restricted T cell responses of the H-2b,d,q,u but not the H-2f,k,s haplotypes, indicating that this xenoantibody recognizes a polymorphic determinant on mouse Ia molecules. This same monoclonal antibody was found to inhibit BALB/c(H-2d) T cell proliferation to both G60A30T10 and G58L38phi4. The Ir genes regulating responses to these antigens map to either the I-A subregion (GAT), or the I-A and I-E subregions (GLphi), raising the possibility that M5/114 recognizes both I-A and I-E subregion-encoded Ia glycoproteins. It could be shown, using appropriate F1 responding cells, that M5/114 does in fact affect GAT and GLphi responses by interaction with both the I-A and the I-E subregion products, and not by an nonspecific effect resulting from binding to the I-A subregion product alone. These results are consistent with genetic and biochemical studies directly demonstrating that M5/114 recognizes AalphaAbeta and EalphaEbeta molecular complexes. The existence of a shared epitope on I-A and I-E subregion products suggests the possibility that these molecules arose by gene duplication. Finally, the precise correlation between the Ia molecules recognized by M5/114 and the ability of this antibody to block T cell responses under Ir gene control strengthens the hypothesis that Ia antigens are Ir gene products. (Author abstract) (33 Refs)

40. EFFECT OF A MONOCLONAL ANTI-LARGE GRANULAR LYMPHOCYTE ANTIBODY ON THE HUMAN NK ACTIVITY.

Nieminen P, Paasivuo R, Saksela E
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J Immunol; 128(3):1097-1101 1982

A monoclonal hybridoma antibody of IgGIa subclass was produced by fusing NS-1 myeloma cells with spleen cells of a mouse immunized with human LGL cells. This hybridoma antibody, termed NK-8, was reactive by indirect immunofluorescence with 33% of peripheral blood LGL cells and 70% of LGL forming conjugates with K-562 cells. Monocytes, granulocytes, and other lymphocytes were nonreactive. In iodinated protein A binding assays NK-8 was nonreactive with all kinds of leukemia and lymphoma lines tested and showed activity only against LGL cells. NK-8 inhibited the LGL-mediated cytotoxicity against K-562 cells by 50 to 60% without complement and inhibited the K-562 induced interferon production from the LGL population. However, the spontaneous cytotoxicity against human skin fibroblasts was augmented if the effector cells were pretreated with NK-8. (Author abstract) (17 Refs)

41. RELATIONSHIP BETWEEN CELL-MEDIATED AND HUMORAL IMMUNE ATTACK ON TUMOR CELLS. II. THE ROLE OF CELLULAR LIPID METABOLISM AND CELL SURFACE CHARGE IN THE OUTCOME OF IMMUNE ATTACK.

Schlager SI
Dept. Microbiology, Univ. Notre Dame, Notre Dame, IN, 46556
Cell Immunol; 66(2):300-316 1982

Treatment of P815 tumor cells with adriamycin increased their sensitivity to killing by anti-P815 antibody plus C, but not by allogeneic P815-sensitized spleen cells. Conversely, mitomycin C treatment enhanced the cells' sensitivity to cell-mediated, but not antibody-C, killing. Hydrocortisone, but not epinephrine, was effective in increasing the resistance of the cells to killing by both antibody- C and cell-mediated attack systems. The ability of the tumor cells to resist antibody-C killing correlated with their ability to incorporate fatty acid into complex cellular lipid; no such correlation was found between the cellular lipid synthesis and tumor cell susceptibility to cell-mediated killing. Drug or hormone-treated tumor cells exhibited unique changes in cellular lipid synthesis and composition and in cell surface physical properties that correlated with their susceptibility to antibody-C or cell-mediated attack. Cells increased in their sensitivity to antibody-C killing exhibited a decreased cholesterol:phospholipid mole ratio. In contrast, cells rendered more sensitive to cell-mediated killing exhibited an increase in polar phospholipid content and a measurable decrease in net negative cell surface charge density. These data implicate unique chemical and/or physical properties of tumor cells to be of fundamental importance for their ability to resist either humoral or cell-mediated immunologic attack; modulation of one or another of these cellular properties results in a change in the cells' susceptibility to immune killing by antibody plus C or by cytotoxic T lymphocytes. (Author abstract) (24 Refs)

42. DIFFERENTIAL VARIATIONS OF SENSITIVITIES OF TNP-MODIFIED LYMPHOMA CELLS TO LYSIS BY CYTOTOXIC LYMPHOCYTES AND BY ANTIBODIES.

Bischoff P, Maugaras M, Oth D
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Immunol Lett; 4(2):107-111 1982

The susceptibility of a well-defined target cell line, towards both cell-mediated lysis and antibody plus complement lysis was compared under fully parallel experimental situations. Cultured RDM4 lymphoma cells were modified with 1 milliM trinitrobenzene sulfonate (TNBS) and assayed for lysis by either in vitro generated cytotoxic T-lymphocytes (CTL) or complement-mediated humoral immunity. The lytic effect of CTL was always greater in the 'youngest' cells (those in exponential growth, as shown by marked incorporation of (3H)thymidine [TdR]) than in cultures in which cells were in the resting phase. In some experiments, RDM4 cells were harvested after 1-4 days of culture and labeled with (3H)TdR or (14C)TNBS. The oldest cells incorporated less (3H)TdR than the youngest cells, but bound more (14C)TNBS to their surface. It is concluded that the efficiency of the CTL on the hapten (trinitrophenyl [TNP])-modified cells is not proportional to the density of TNP-groups on the targets, and that CTL on the one hand, and complement-mediated humoral immunity on the other hand, must have different cell surface requirements to be able to lyse the target cells. (16 Refs)

43. SQUAMOUS CELL CARCINOMA ASSOCIATED WITH DISTURBANCE OF THE IGA SYSTEM.

Furukawa F, Taniguchi S, Danno K, Komura J, Mizumoto T, Kanoh T
Dept. Dermatology, Faculty Medicine, Kyoto Univ., Sakyo, Kyoto 606, Japan
Dermatologica; 164(1):30-35 1982

A case of squamous cell carcinoma of the skin associated with disturbance of the IgA system is described. Immunological observations revealed a marked low level of serum IgA and disturbance of the secretory IgA synthesis in the rectal mucosa. After the surgical removal of the skin tumor, the serum level of IgA was increased to half the normal-range level. The relationship of the disturbance of the IgA system to the occurrence of squamous cell carcinoma is discussed. (Author abstract) (12 Refs)

44. ALTERATION OF LYMPHOID CELLS IN AKR MICE BY TREATMENT WITH MONOCLONAL ANTIBODY AGAINST THY-1 ANTIGEN.

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Genetic Systems Corporation, 3005 First Ave., Seattle, WA, 98121
Transplantation; 33(3):269-273 1982

AKR/J mice treated with high levels of monoclonal anti-Thy-1.1 antibody and C' remained healthy without apparent side effects. Examination of the lymphatic organs of these mice demonstrated a selective depletion of T cells in lymph nodes and spleen. Following cessation of treatment of the levels of anti-Thy-1.1 antibody in the circulation fell and the peripheral lymphatic organs gradually became repopulated with T cells. Depletion occurred in lymph nodes whether or not C' was infused along with the antibody. Although the thymocytes of these mice were coated with anti-Thy-1.1 antibody they were not eliminated by the treatment. The elimination of peripheral but not thymic T cells suggests either a thymic barrier to the penetration of cofactors (possibly antibody-dependent effector cells) or that antibody acts by interfering with the normal traffic of peripheral T cells which normally 'home' to the lymph nodes and spleen. (Author abstract) (9 Refs)

45. EX VIVO PERFUSION OF HUMAN COLON WITH MONOCLONAL ANTICOLORECTAL CANCER ANTIBODIES.

Sears HF, Herlyn D, Herlyn M, Steplewski Z, Grotzinger P, Koprowski H
Fox Chase Cancer Center, Central and Shelmire Ave., Philadelphia, PA, 19111
Cancer; 49(6):1231-1235 1982

The binding of mouse hybridoma monoclonal antibodies directed against human colon carcinomas was studied using an ex vivo perfusion model of a freshly resected human colon segment containing a carcinoma. Tumor and the surrounding normal bowel is exposed to the putative tumor antigen through an intact vascular system without mechanical or enzymatic cellular alteration. An hour of perfusion was conducted on 30 specimens using five different monoclonal anticolorectal cancer (ACRC) antibodies. Three were gamma1, one gamma2A and one was IgM isotype. Control anti-influenza virus monoclonal antibodies were used to demonstrate absence of nonspecific binding. Our antibody 17-1A bound to the colon cancer in 7 of 10 trials, but bound to normal colon cells also in 4 of these trials. The IgM antibody did not bind to anything. The two gamma1 antibodies that recognize an antigen shed from the surface of the cell did not demonstrate cell binding under conditions of this study, and conditions to detect this will have to be modified. The ex vivo perfusion model as performed in this study can provide a valuable adjunct to evaluate the potential clinical utility for antibody conjugate radiolocalization or therapy of colon cancer. (Author abstract) (10 Refs)

46. ANTIBODIES CONJUGATED TO POTENT CYTOTOXINS AS SPECIFIC ANTITUMOR AGENTS.

Moolten FL, Schreiber BM, Zajdel SH
Boston Univ. Sch. Medicine, Boston, MA
Immunol Rev; 62:47-73 1982

The ability of toxins, enzymes, radioisotopes, and cytotoxic drugs linked to antibodies to selectively kill cells bearing surface antigens that are targets for the antibodies is reviewed. Criteria for the complexes include the following: the cytotoxin must be capable of acting after delivery to the cell surface by the antibody, the desired biologic properties of the components must survive the conjugation process, the conjugate must be stable until delivered to its site of action, the specificity of the conjugate must reflect primarily the specificity of the antibody complex, and the toxic moiety must be extraordinarily potent. Conjugates tested for antitumor activity include diphtheria toxin conjugates, Pseudomonas aeruginosa toxin conjugates, ricin conjugates, and phospholipase and ribonuclease conjugates. In vitro, each of the agents, when conjugated to antibodies directed against a variety of cell-surface antigens, was selectively cytotoxic to cells bearing those antigens. In vivo, diphtheria toxin conjugated to antibodies directed against the dinitrophenol (DNP) hapten reduced the incidence and growth rate of tumors in hamsters concurrently inoculated with DNP-coated sarcoma cells. When tested against a more sensitive Simian virus 40-induced tumor, two conjugate preparations induced permanent regressions of established tumor in 20% and 56% of treated hamsters. (65 Refs)

47. UNIVALENT ANTIBODIES KILL TUMOUR CELLS IN VITRO AND IN VIVO.

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Nature; 295(5851):712-714 1982

The use of univalent antibodies to kill tumor cells in vitro and in vivo was studied. L2C cells were obtained from the blood of near-terminal guinea pigs bearing L2C lymphocytic leukemia. Two antibodies against L2C cells were raised in rabbits: one against the lambda chain of L2C surface immunoglobulin (anti-L) and one against idiotypic determinants of the surface immunoglobulin (anti-Id). Univalent Fab/c derivatives of both antibodies were prepared by digestion with thiol-free papain. Anti-L and anti-Id both bound to the surfaces of L2C cells in vitro, as shown by indirect immunofluorescence assay. Although parent bivalent anti-L and anti-ID underwent redistribution and endocytosis on the surface of L2C cells and rendered the cells resistant to lysis, the Fab/c derivatives did not. The derivatives were able to evoke complement-mediated lysis of L2C cells and did not tend to induce antigenic modulation. Both derivatives were superior to bivalent IgG in bringing about cell lysis. When tested in vivo against L2C tumor cells with a doubling time of approx 19 hr, Fab/c lengthened survival of guinea pigs by 10 days. Results indicate that bivalency of IgG plays an important role in allowing tumor cells to escape antibody-mediated lysis. Therapeutic value of univalent antibodies is suggested for treatment of human cancers. (20 Refs)

48. TREATMENT OF B-CELL LYMPHOMA WITH MONOCLONAL ANTI-IDIOTYPE ANTIBODY.

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N Engl J Med; 306(9):517-522 1982

A 67-yr-old man with nodular, poorly differentiated, lymphocytic malignant lymphoma was treated with monoclonal anti-idiotype antibody. Partial responses were produced with leukocyte interferon and chemotherapy (cyclophosphamide, vincristine, and prednisone). Progressive lymphoma refractive to chemotherapy was shown by biopsy to be diffuse, poorly differentiated lymphocytic lymphoma. Anti-idiotype antibody (4D6) was given in a continuous 6-hr infusion. Plasmapheresis did not reduce the idiotype level. With 15 mg anti-idiotype antibody, a dramatic decrease in the idiotype level was noted. No toxicity or side effects were observed. Doses of 40 and 75 mg caused progressively greater decreases in serum idiotype; after 150 mg idiotype levels remained undetectable. The detectability of anti-idiotype coincided with the disappearance of serum idiotype. No measurable tumor response was noted after five doses of anti-idiotype; however, anti-idiotype penetrated and bound to cells within the lymph node. The patient's condition improved following four injections of 4D6, measurable tumor response occurred after the 75-mg dose, and over the next 3 wk the patient's enlarged lymph nodes gradually became smaller. The liver and spleen returned to normal size, tumors on the scalp disappeared, and platelet count and Hb rose to normal levels. Treatment was discontinued after a total of eight doses of antibody over 4 wk. The patient has remained in remission without further therapy for greater than 6 mo. (20 Refs)

IMMUNOGLOBULIN STRUCTURE AND SYNTHESIS

49. IMMUNOGLOBULIN HEAVY-CHAIN EXPRESSION AND CLASS SWITCHING IN A MURINE LEUKAEMIA CELL LINE.

Alt FW, Rosenberg N, Casanova RJ, Thomas E, Baltimore D
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Nature; 296(5855):325-331 1982

A cell line that switches from mu to gamma2b synthesis during growth in culture uses the same VH region for both heavy chains but retains two copies of the Cu gene. This suggests that the mu to gamma2b class switch can occur, at least in part, by an RNA processing mechanism. Regulatory variants of this cell line lose constitutive mu-chain synthesis but simultaneously acquire lipopolysaccharide (LPS)-inducible synthesis of that chain. This co-variation is allele-specific and is correlated to a large deletion of DNA in the JH-Cmu intron. (Author abstract) (42 Refs)

50. RECOMBINED FLANKS OF THE VARIABLE AND JOINING SEGMENTS OF IMMUNOGLOBULIN GENES.

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Proc Natl Acad Sci USA; 79(5):1383-1387 1982

The mechanism of generating immunoglobulin light chain genes by rearrangement of variable (V), joining (J), and constant (C) gene segments is still unknown. It has been discussed mostly in terms of excision and deletion of the DNA between the recombined V and J gene segments. However, the finding in DNA digests from the mouse myeloma T of a fragment (called f-T) that contains the 3' flank of a V kappa and a 5' flank of a J1 gene segment argued against a simple deletion mechanism. The origin of fragment f-T has now been investigated by cloning and determining the sequence of the germline V gene segment that apparently participated in its formation. Moreover, analogous fragments containing flanking sequences were isolated from the myelomas MOPC 173 and 41 (f-173 and f-41) and studied by sequence analysis. The f fragments appear to be recombination products of V-J rearrangements reciprocal to rearranged kappa genes but, at least in the cases of f-T and f-173, not of the rearranged V genes present in the same tumor cell. This fact is best explained by a sister chromatid exchange mechanism of V-J recombination because, by this model, the rearranged V genes and the reciprocal flank recombination products would segregate into different cells during the following mitosis. The possibility is suggested that there exists in lymphocyte differentiation more than one mechanism of V-J recombination. (Author abstract) (27 Refs)

51. ANTIGEN-INDEPENDENT, IGM-INDUCED ANTIBODY RESPONSES: REQUIREMENT FOR 'RECURRENT' IDIOTYPES.

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Eur J Immunol; 12(2):146-151 1982

Anti-idiotypic antibodies (a-Id) were produced in syngeneic mice against two monoclonal IgM antibodies of BALB/c origin, TNP.11 and SP/603. In plaque inhibition tests, using IgM-secreting hybridoma cells and anti-idiotypic antibodies, these two IgM proteins, as well as the anti-TNP myeloma protein MOPC 460 (IgA) were found to carry non-cross-reactive idiotypes. Analysis of the anti-trinitrophenyl (TNP) plaque-forming cells (PFC) in BALB/c mice, either normal or immunized with TNP-horse red blood cells, revealed that in addition to the MOPC 460 Id, also the SP/603 Id is recurrent and expressed by a fraction of the anti-TNP antibody-secreting cells in all individuals tested. In contrast, the TNP.11 Id could not be detected in any BALB/c mouse studied. TNP.11 and SP/603 antibodies were then characterized by their ability to induce an antigen-independent anti-TNP response in normal BALB/c mice. While TNP.11 was found to be inactive, the same titers of SP/603 IgM induced antigen-specific PFC all of which expressed the SP/603 Id, and increased titers of circulating IgM molecules carrying the same Id, suggesting that 'recurrent' but not 'nonrecurrent' Id are competent in this respect. A fraction of these SP/603-induced, SP/603-positive anti-TNP antibodies also carried MOPC 460 Id, suggesting expression on the same molecule of idiotypic determinants found on independent non-cross-reactive 'recurrent' idiotypes. (Author abstract) (30 Refs)

52. FC RECEPTORS OF MOUSE CELL LINES. II. IGG BINDING SPECIFICITY AND IDENTIFICATION OF THE FC RECEPTOR ON A LYMPHOID LEUKEMIA.

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J Immunol; 128(4):1825-1831 1982

We determined the binding specificity of the Fc receptors on the murine lymphoid leukemia, L1210, which bears several surface antigens characteristic of B cells and B cell precursors. L1210 possesses an Fc receptor that binds monomer IgG of the IgG1, IgG2a, and IgG2b subclasses with low affinity, whereas aggregated IgG of these subclasses is bound comparatively well. There was no detectable binding of monomer or aggregated IgG3. Although direct binding of monomer IgG was difficult to demonstrate, monomer inhibition of aggregate binding was found at monomer concentrations in excess of 0.2 mg/ml. There was cross-competition between monomers and aggregates of all three subclasses, indicating that all were binding to the same Fc receptor. Isolation and characterization of the Fc receptor of L1210 was accomplished by affinity chromatography of the radiolabeled cell lysate over columns of Sepharose 4B coupled to various IgG and control proteins. A single protein, with an approx mw of 60,000, was found to specifically bind to the Fc portion of IgG. This protein was demonstrated in the acetic acid and SDS eluates from columns coupled to monomer, aggregated, or antigen-complexed IgG, but was not seen in eluates from F(ab')2 columns or from eluates of IgG columns that received the lysates of Fc receptor-negative cells. The 60-kd Fc binding protein was also demonstrated in the SDS eluates from affinity columns of Sepharose 4B coupled to myeloma proteins of mouse IgG1, IgG2a, and IgG2b subclasses. These studies indicate that in contrast to mouse macrophage-like cell lines that possess separate IgG subclass specific Fc receptors, L1210, a murine leukemia of possible B cell lineage, possesses a single Fc receptor with distinct binding and structural characteristics. (Author abstract) (40 Refs)

53. CONTROL OF IGM SYNTHESIS IN THE MURINE PRE-B CELL LINE, 70Z/3.

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J Immunol; 128(4):1664-1670 1982

The murine 70Z/3 tumor resembles a pre-B cell in synthesizing only intracellular chains and no detectable light chain. However, one kappa gene is already rearranged, and after overnight incubation with lipopolysaccharide (LPS), most of the cells are induced to synthesize light chain. The induced cells display IgM on their surface, but do not secrete IgM. Thus, 70Z/3 cells resemble cells poised at the pre-B cell/B lymphocyte border. We have examined synthesis and post-translational modification of mu-chains in uninduced and induced 70Z/3 cells. Isolation of mu-chains and peptide maps demonstrated that both populations synthesize intracellular forms that correspond to membrane-specific mum and secretion-specific mus chains. These intracellular forms have completed only the first of the two glycosylation steps characteristic of eukaryotic cells. After induction by LPS, L chain synthesis commences, mum and mus synthesis are both increased twofold to threefold (due to an increased rate of synthesis rather than decreased degradation), and both complex with L chain to form mu2L2 tetramers. Furthermore, the glycosylation of a subset of the mum chains is completed, and these are placed on the membrane. However, unglycosylated mu2L2 tetramers can be placed on the membrane, so glycosylation is not a requirement. These data suggest that L chain may not be sufficient for externalization of mum and mus chains. These data support the idea that the controls of membrane placement and secretion of mu chains are post-translational and that different mechanisms operate for mum and mus chains. (Author abstract) (61 Refs)

54. COMMUNICATIVE INTERACTIONS BETWEEN SUBPOPULATIONS OF HUMAN T LYMPHOCYTES REQUIRED FOR GENERATION OF SUPPRESSOR EFFECTOR FUNCTION IN A PRIMARY ANTIBODY RESPONSE.

Morimoto C, Distaso JA, Borel Y, Schlossman SF, Reinherz EL
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J Immunol; 128(4):1645-1650 1982

The cellular interactions necessary for generation of human T suppressor effector function were examined in a primary in vitro antigen-specific anti-DNP antibody-forming system. During the induction of the anti-DNP response, it was found that T cells of both T4+ and T8+ subsets were necessary to suppress antibody formation, whereas after activation, only the T8+ subset was required. Thus, a population of T4+ T cells appears to be necessary to activate or induce a subset of T8+ cells to suppress. The T4+ suppressor inducer population, like the resting or activated T8+ suppressor effector subset, was sensitive to low dose irradiation. Moreover, the radiosensitive T4+ subset and the previously defined T4+JRA+ subset were shown to be functionally similar or complementary in that both were required for generation of suppressor effector function. These findings suggest that T-T interactions between radiosensitive T4+JRA+ T cells and radiosensitive T8+ T cells are necessary for suppression of primary antigen-specific antibody production in man. (Author abstract) (30 Refs)

55. THE INVOLVEMENT OF TWO DISTINCT SUBSETS OF T CELLS FOR THE EXPRESSION OF THE IGE CLASS-SPECIFIC SUPPRESSION: ESTABLISHMENT AND CHARACTERIZATION OF PC-SPECIFIC, T15 IDIOTYPE-POSITIVE T HYBRIDOMAS AND IGE CLASS-SPECIFIC, ANTIGEN-NONSPECIFIC T HYBRIDOMAS.

Sugimura K, Nakanishi K, Maeda K, Kashiwamura SI, Suemura M, Shiho O, Yamamura Y, Kishimoto T
Third Dept. Medicine, Osaka Univ. Medical Sch., Fukushima-ku, Osaka 553, Japan
J Immunol; 128(4):1637-1644 1982

PC-Myc-primed T cells showed PC-specific suppressor function selectively on the IgE antibody response. Treatment of PC-Myc-primed T cells with anti-T15 idiotypic antibody and complement abolished the IgE class-specific suppressor function and the suppressor effect of PC-Myc-primed T cells could be enriched by employing anti-T15 idiotypic antibody-coated petri dishes, showing the involvement of T15 idiotype-positive T cells in the IgE class-specific suppression. Somatic cell hybridization of PC-Myc-primed T cells with BW5147 could give rise to two distinct types of hybridomas, ie, PC-specific and IgE class-specific. PC-specific hybridomas were stained with anti-T15 idiotypic antibody and showed rosette formation with PC-SRBC, which was inhibited by the addition of anti-T15 idiotypic antibody. The culture supernatant obtained from these hybridomas showed a PC-specific suppressor effect on the IgE, as well as IgG, responses. PC-binding molecules could be isolated from the surface-labeled PC-specific hybridomas by affinity chromatography and their mw was approx 64,000 by SDS-PAGE analysis. On the other hand, IgE class-specific hybridomas did not express any PC-binding molecules when tested by immunofluorescence or the rosette formation. No PC-binding molecules could be isolated from these cells by employing the same conditions applied to PC-specific hybridomas. The culture supernatant showed the antigen-nonspecific suppressor function selectively on the IgE response. When taken collectively, these results suggest the involvement of two distinct subsets of T cells for the expression of the IgE class-specific suppression. (Author abstract) (37 Refs)

56. MITOGEN-STIMULATED IMMUNOGLOBULIN PRODUCTION BY CHRONIC LYMPHOCYTIC LEUKAEMIC LYMPHOCYTES.

Johnstone AP, Jensenius JC, Millard RE, Hudson L
Dept. Immanology, St. George's Hosp. Medical Sch., London SW17 0RE, England
Clin Exp Immunol; 47(3):697-705 1982

The capacity of B cells from patients with chronic lymphocytic leukemia (CLL) to produce and secrete immunoglobulin following mitogen stimulation was investigated using sensitive radioimmunoassays for mu, gamma, alpha, kappa and lambda immunoglobulin chains. Lymphocytes from 7 of the 11 patients studied secreted immunoglobulin in response to pokeweed mitogen (PWM). IgM was always the major immunoglobulin and in five of the seven responders it was the only class detected; only one type of light chain was observed in most cases. This was in contrast to normal lymphocytes which secreted all classes of immunoglobulin (IgM was invariably the lowest) containing both types of light chain. Lipopolysaccharide induced immunoglobulin secretion in only one of four CLL cases. This was again IgM with only one type of light chain. The assays are therefore most probably measuring a response by the leukemic cells. In most CLL cases, immunoglobulin secretion by the residual normal cells, which proliferate in response to mitogen, was not observed. This inability of the normal lymphocytes to differentiate fully into immunoglobulin secreting cells and the block in switching from IgM production to other classes in the leukemic cells may both be attributable to a defect in the regulatory system of the immune response in CLL patients. (Author abstract) (22 Refs)

57. T-CHRONIC LYMPHOCYTIC LEUKAEMIA PRESENTING AS PRIMARY HYPOGAMMAGLOBULINAEMIA - EVIDENCE OF A PROLIFERATION OF T-SUPPRESSOR CELLS.

Thien SL, Catovsky D, Oscier D, Goldman JM, Van Der Reijden HJ, Melief CJ, Rumke HC, Ten Berge RJ, Von Dem Borne AE
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Clin Exp Immunol; 47(3):670-676 1982

A 63-yr-old man with late onset hypogammaglobulinemia is described. Splenectomy, carried out because of marked splenomegaly and pancytopenia, demonstrated marked T lymphocytic infiltration in the splenic red pulp with prominent germinal centers. A persistent peripheral blood and bone marrow lymphocytosis ensued (10 x 10(9)/l and 40% respectively) and this was consistent with T-chronic lymphocytic leukemia (T-CLL). Over 88% of his blood lymphocytes were E+, OKT3+, OKT8+ and OKT11+; 54% of the T lymphocytes had receptors for IgG (Tgamma cells). Functional studies showed that the T lymphocytes of this parent lacked killer and natural killer cell function but they effectively suppressed the differentiation of norm al B cells in a PWM stimulated system. It is suggested that the T-CLL in this patient resulted from the proliferation of the T suppressor subset which was responsible for his hypogammaglobulinemia. (Author abstract) (21 Refs)

58. CORRELATION BETWEEN D REGION STRUCTURE AND ANTIGEN-BINDING SPECIFICITY: EVIDENCES FROM THE COMPARISON OF CLOSELY RELATED IMMUNOGLOBULIN VH SEQUENCES.

Auffray C, Sikorav JL, Ollo R, Rougeon F
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Ann Immunol (Paris); 132(1):77-88 1981

Complementary DNA (cDNA) clones containing VH sequences of three myeloma proteins, of which two (UPC10 and ABE48) bind 2,6-levan, and one (MOPC173) has an unknown specificity, were constructed and sequenced. cDNA clones were compared to four sequences of anti-galactan myeloma proteins belonging to NIH BALB/c plasmacytoma. Starting with partially purified alpha heavy chain messenger RNA (mRNA) from ABE48 myeloma and gamma2a heavy chain mRNA from MOPC173 myeloma, collections of recombinant plasmids were constructed. Plasmids palpha48-16 and pG2a-173-27, which carry the most important part of the corresponding VH sequences were isolated using 650-base pair PstI fragment of pG2a-10-21 containing the VH sequence. Nucleotide sequences are presented. As a result of the cloning procedure, the sequence corresponding to the 5' end of the mRNA is not present in pG2a-173-27, which begins at the codon 5 of the variable region of the heavy chian (VH region), and in palpha48-16, which begins at codon 32 of the VH region. The amino-acid sequences presented were derived from the nucleotide sequences. The MOPC173 sequence agrees with a previously reported except for the exchange Asn/Asp at codons 52-54 and 73-74. Results confirm the strong correlation existing between D-region structure and antigen-binding specificity. (29 Refs)

59. MEMBRANE-BOUND AND CELLULAR IMMUNOGLOBULINS IN HUMAN B-LYMPHOMA LINES AND DERIVED HYBRIDS.

Spira G, Aman P, Silvian I, Koide N, Ber R, Klein G
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Immunobiology; 160(3/4):340-351 1981

Hybrids derived from the fusion of cell lines representing different maturation stages were studied for their membrane and cellular immunoglobulin expression. The hybrids can be subdivided into three groups, with one common parental line in each group. In the first group, Raji cells represent the common parent: it contains small amounts of membrane and cytoplasmic mu and kappa chains. In the second group, PUT is the common parent, an ouabain and TG-resistant subline of the BL-derived P3HR-1 line. PUT contains a truncated intracellular mu chain. The third group consists of hybrids between K562, an EBV-negative human erythroleukemia line and two different BL lines. Membrane-immunoglobulin expression was intermediate between the parental lines in the first two groups derived from the fusion of two BL lines. In the third group, hybridization with the K562 cell suppressed the membrane-Ig expression of the B-cell partner. Total cellular immunoglobulin determinations showed that some cells synthesized light chains in excess of heavy chains, others contained an excess of heavy chains, while still others had equal amounts of heavy and light chains. The hybrids showed a variety of patterns, including amplification of the parental phenotypes, appearance of new phenotypic combinations, and eclipse of one or both parental phenotypes. A comparison of the total and the membrane-associated immunoglobulin patterns suggests independent handling of intracellular and membrane immunoglobulin synthesis. (Author abstract) (28 Refs)

60. TRANSPORT OF AN IMMUNOGLOBULIN LIGHT CHAIN FRAGMENT ACROSS THE ENDOPLASMIC RETICULUM DOES NOT REQUIRE AN AMINO TERMINAL VARIABLE REGION: IMPLICATIONS FOR THE SIGNAL HYPOTHESIS.

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Biochem Biophys Res Commun; 104(4):1630-1637 1982

The co-translational processing of the kappa light chain constant region fragment was studied in a Krebs ascites cell-free system. The fragment (which is devoid of the entire variable region) was initially synthesized as a precursor which contains a signal (pre) peptide. In the presence of microsomal membranes, the pre-peptide was removed and the cleaved fragment was transported into the vesicles. NH2-terminal sequences normally adjacent to the signal peptide of a kappa light chain were not necessary for translocation. (23 Refs)

61. THE DIFFERENTIAL ULTRASTRUCTURAL LOCALIZATION OF IMMUNOGLOBULIN HEAVY AND LIGHT CHAINS IN HUMAN HAEMATOPOIETIC CELL LINES.

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Br J Haematol: 50(3):445-459 1982

The ultrastructural localization of immunoglobulin heavy and light chains has been investigated in nine hematopoietic cell lines, using a technique which involves the treatment of lightly prefixed cells with saponin to allow penetration of the antibody-peroxidase conjugates. The synthesis and secretion of immunoglobulin was also studied in these cell lines. Immunoglobulin was found to be localized in the cisternae and on the membranes of the rough endoplasmic reticulum, perinuclear space and/or Golgi apparatus. In each case staining for heavy chains was weak or absent in the perinuclear space while staining for light chains was usually strong. Additionally in three cell lines immunoperoxidase staining indicated that heavy chains were absent from the Golgi apparatus despite the observed presence of light chains in the Golgi apparatus and the secretion of combined immunoglobulin into the supernatant. The results obtained suggest compartmentalization of the synthesis of light and heavy chains and indicate that the technique of immunoelectron microscopy may significantly contribute to an understanding of the mechanisms involved in immunoglobulin synthesis, intracellular transport and secretion. (Author abstract) (25 Refs)

62. SWITCH FROM NP-SPECIFIC IGG3 TO IGG1 IN THE MOUSE HYBRIDOMA CELL LINE S24/63/63.

Baumhackel H, Liesegang B, Radbruch A, Rajewsky K, Sablitzky F
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J Immunol; 128(3):1217-1220 1982

We have isolated by fluorescence-activated cell sorting an IgG1 expressing class switch variant (S24-1/47) from the IgG3-producing mouse hybridoma cell line S24/63/63. Both Ig bind the hapten 4-hydroxy-3-nitro-phenylacetyl (NP) with approx the same affinity and fine specificity and are idiotypically indistinguishable. The apparent mw is 50,000 for the gamma1 and 51,000 for the gamma3 chain. The genomic DNA of IgG3-producing S24/63/63 cells contains a 14-kb Eco RI restriction fragment with C-gamma3 sequences representing a rearranged Cgamma3 gene. In the class switch variant S24-1/47 the Cgamma3 gene is deleted. (Author abstract) (22 Refs)

63. ULTRASTRUCTURAL EVENTS IN THE TRANSLOCATION OF POLYMERIC IGA BY RAT HEPATOCYTES.

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J Immunol; 128(3):1181-1187 1982

It has been proposed that polymeric IgA is translocated from plasma to bile across hepatocytes of the rat liver by a secretory component-mediated, vesicular transport. To define the ultrastructural details of the proposed transport mechanism, we employed peroxidase-labeled antibody immunocytochemistry to localize secretory component in the rat liver and monitor the hepatic translocation of homologous myeloma polymeric IgA infused iv. Secretory component was found associated with the endoplasmic reticulum, Golgi complexes, cytoplasmic vesicles, and plasma membranes of the sinusoidal and canalicular surfaces of hepatocytes; secretory component at the sinusoidal surface was most prominent in micropinocytic invaginations or pits. Livers were examined for the sites of polymeric IgA 5, 15, and 30 min after infusion. Evidence was obtained that polymeric IgA is translocated across hepatocytes by a series of events: (1) polymeric IgA binds selectively to secretory component on the external surface of the sinusoidal plasma membrane; (2) secretory component-IgA complexes are internalized in endocytic vesicles; (3) the vesicles migrate through the cytoplasm without association with lysosomes or Golgi complexes; (4) the vesicles fuse with the cytoplasmic surface of the bile canalicular membrane, where secretory component-IgA complexes are released into bile by exocytosis. (Author abstract) (47 Refs)

64. ACTIVATION OF SUPPRESSOR T CELLS BY AUTOLOGOUS LYMPHOBLASTOID CELLS: A MECHANISM FOR FEEDBACK REGULATION OF IMMUNOGLOBULIN SYNTHESIS.

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Immunophysiology Section, Metabolism Branch, NCI, NIH, Bethesda, MD, 20205
J Immunol; 128(3):1149-1154 1982

In this study, the regulatory potential of T cells activated as a result of exposure to autologous lymphoblastoid cells was examined. In initial studies it was observed that the proliferative response of T cells induced by exposure to mitogen-transformed or Epstein Barr virus (EBV)-transformed autologous lymphoblastoid cells was greater than the proliferative response of T cells induced by exposure to unstimulated autologous B cells. Such activated T cells profoundly suppressed pokeweed mitogen (PWM)-stimulated immunoglobulin synthesis by autologous indicator cells, but compared to fresh T cells or cultured T cells, these activated cells had a diminished capacity to provide help for PWM-stimulated immunoglobulin synthesis. In additional studies it was found that (1) both PWM-transformed B cells and EBV-transformed B cells were able to activate suppressor T cells, suggesting that the mechanism of activation is independent of the agent used to transform the lymphoid cells; (2) T cells cultured with PWM-induced lymphoblastoid cells did not suppress immunoglobulin synthesis when added to PWM-stimulated cells after 3 days of culture, indicating that suppression was not due to killing of immunoglobulin-secreting cells; (3) mitogen-induced lymphoblastoid cells acquired maximal ability to activate suppressor T cells after 3 days of culture with the mitogen, indicating that lymphoid cells had to undergo mitogen-induced changes to activate suppressor T cells. These results are compatible with the concept that when B cells are activated to differentiate into immunoglobulin-secreting cells, they express new determinants that are capable of activating suppressor T cells, which can then act to inhibit further B cell differentiation. (Author abstract) (26 Refs)

65. IMMUNOGENETICS OF BCG-INDUCED ANERGY IN MICE; CONTROL BY GENES LINKED TO THE IGH COMPLEX.

Schrier DJ, Sternick JL, Allen EM, Moore VL
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J Immunol; 128(3):1466-1469 1982

The genetics of BCG-induced anergy was studied in mice by evaluating delayed hypersensitivity to sheep erythrocytes. Data obtained using congenic mice and by linkage analysis suggested that genes linked to the H-2 complex do not influence the development of anergy. However, studies in allotype-congenic partners (BALB/c; BALB.Igb) indicated that anergy was influenced by genes linked to the immunoglobulin heavy chain complex (Igh). Breeding studies indicated that the gene influencing anergy is recessive. These studies were extended by using BXD recombinant inbred mice and verified that anergy is controlled by genes linked to the Igh complex. Because several markers and a tentative map have been constructed for the Igh complex on chromosome 12 in BXD mice, we suggest that the gene that controls BCG-induced anergy is located on the centrometric side of Igh-C approximately 18 to 28 recombination units. (Author abstract) (40 Refs)

66. TUMOR PROMOTOR PHORBOL MYRISTIC ACETATE IS A T-CELL-DEPENDENT INDUCER OF IMMUNOGLOBULIN SECRETION IN HUMAN LYMPHOCYTES.

Ralph P, Kishimoto T
Developmental Hematopoiesis, Memorial Sloan-Kettering Cancer Center, Rye, NY, 10580
Clin Immunol Immunopathol; 22(3):340-348 1982

Human peripheral blood mononuclear cells were induced by 10 to 200 ng/ml phorbol myristic acetate (PMA) to secrete immunoglobulin (Ig). Using protein A-RBC plaque formation to detect secreting cells (PFC), Day 5 and Day 7 PFC induced by PMA were 0.2 to 1.4% of initial numbers of cultured cells. In parallel cultures, pokeweed mitogen (PWM) induced PFC corresponding to 1-3% and 0.6-8% of initial cell numbers, respectively. Suppressor cells for Ig secretion purifying with T (E-rosetting) cells were found in most donors. These were sensitive to mitomycin C. In some donors, PFC responses could only be detected after removal of suppressor cells. By double separation of T cells from B cells, the PMA response was shown to be dependent on T helper cells, similarly to PWM. This is in contrast to a 20-fold stimulation of Ig secretion in some human B culture lines by PMA alone. PMA is thus a T-dependent polyclonal activator for resting, blood B lymphocytes, and a direct stimulator of Ig production in certain dividing lymphoblasts represented by B-cell lines. (Author abstract) (28 Refs)

HUMORAL IMMUNE BLOCKING FACTORS AND ANTIGEN-ANTIBODY COMPLEXES

67. FERRITIN LEVELS AND CIRCULATING IMMUNE COMPLEXES IN PATIENTS WITH SOLID TUMORS.

Celada A, Barnet M, Aguado MT, Cruchaud A, Lambert PH
Div. Hematology RM 10, Dept. Medicine, Univ. Washington, Seattle, WA, 98195
Bull Cancer (Paris); 69(1):22-27 1982

The level of ferritin and circulating immune complexes (IC) were measured in 53 patients with solid tumors and metastasis using C1q binding assay and the conglutinin binding assay. The level of circulating IC was increased in patients (p less than 0.001) as compared to the controls. Ferritin level was increased in both male and female patients (p less than 0.001), even when the ferritin value was corrected by the aspartic transaminase value, to take hepatic damage into account. Ferritin was not found to be an important component of immune complexes as IC ferritin did not exceed 2% of total serum ferritin in the 10 patients that were investigated. These results suggest that ferritin levels and circulating IC are increased in patients with solid tumors and metastasis, but that these two parameters are not correlated. (Author abstract) (29 Refs)

68. IMMUNE COMPLEXES WITH ANTIGLOBULIN ACTIVITY IN SERA OF MOLONEY SARCOMA-BEARING RATS.

Balint J
Dept. Medicine, Baylor Coll. Medicine, Houston, TX, 77030
Clin Exp Immunol; 48(1):70-78 1982

Immune complexes (IC) were detected and isolated from the serum of Brown Norway (BN), (Lewis x BN)F1, and Lewis rats bearing a Moloney sarcoma (MST). IC were isolated from the serum of individual rats employing a system of G-200 chromatography and passage through a heavy chain specific anti-rat IgG Immunoadsorbent. IgG and IgM were identified in the isolated IC by polyacrylamide gel electrophoresis (PAGE) and co-precipitation radioimmunoassays. Employing monospecific antibodies, IC consisting of IgG and IgM were bound to Raji cells as assessed by radioimmunoassay and indirect immunofluorescence. Raji binding activity of IC-containing serum was substantially reduced by pretreatment with dithiothreitol or incubation with anti-rat IgM or pooled normal rat IgG: $F(ab')_2$. Sucrose density gradient ultracentrifugation under acid conditions dissociated IC into 7S IgG and 19S IgM components which recombined when co-incubated at pH 7.5. Viral antigens (gp70 and p30) were not detected in IC by PAGE and co-precipitation radioimmunoassay. Findings show that sera of rats bearing MST contain IC consisting predominantly of immunoglobulin. An IgM component which was separated, isolated and identified within IC containing serum displays anti-$F(ab')_2$ reactivity. (Author abstract) (28 Refs)

69. C1Q SOLID-PHASE ENZYMATIC MICROASSAY FOR DETECTION OF CIRCULATING IMMUNE COMPLEXES: ITS APPLICATION IN HUMAN BREAST CANCER.

Manzo C, Longo C, Bianchin A
Istituto Tumori Fondazione Pascale, Via M. Semmola, Cappella Cangiani, 80131 Napoli, Italy
Tumori; 68(1):47-52 1982

Circulating immune complexes (CIC) were detected and quantitated in human breast cancer to monitor the efficiency of mastectomy. For this aim a microimmunoenzymatic test was set up, applying a solid-phase C1q. Features of this assay can be summarized as follows: ability to estimate as low as 10 ng of aggregated human IgG (deltaIgG), good reproducibility and simplicity of execution, and small serum sample required. A group of women with breast cancer at different stages (TNM classification) was tested for CIC, and 31.75% were positive. Almost all patients submitted to surgery showed a reduction of this parameter thereafter. A parallel study was carried out in another group of women with benign breast disease, and a significant incidence of CIC was found. (Author abstract) (19 Refs)

70. 'HIDDEN' CYTOTOXIC ANTIBODIES THAT REACT WITH ALLOGENEIC CULTURED FETAL AND TUMOR CELLS CONTAINED IN SOLUBLE IMMUNE COMPLEXES FROM NORMAL HUMAN SERA.

Morgan AC, Rossen RD, McCormick KJ, Stehlin JS, Giovanella BC
(c/o Rossen) Immunology Res. Lab., Veterans Admin. Medical Center, Building 211, Room 203, 2002 Holcombe Blvd., Houston, TX, 77211
Cancer Res; 42(3):881-887 1982

Hidden complement-dependent cytotoxins were demonstrated in normal donor sera after removing anti-immunoglobulins that normally block the ability of these immunoglobulin Gs to react with surface antigens on tumor cells. The blocking antibodies had certain properties of anti-idiotypes. Immunoglobulin G from Cohn Fraction II, after removing these anti-immunoglobulins, was cytotoxic for cultured fetal cells and for malignant melanoma, breast, lung, colon, and other tumor cells maintained either in tissue culture or by serial passage in nude mice. The cytotoxins were not adsorbed by extracts from normal lymphoid, liver, skin, or red blood cells. These results suggest that a heterogeneous group of natural antibodies reactive with antigens expressed on a variety of neoplastic and fetal cells circulate in normal donor sera as part of a soluble immune complex, together with a blocking anti-immunoglobulin. (Author abstract) (39 Refs)

71. ERADICATION OF MURINE LYMPHOMA AND MELANOMA CELLS BY CHLORAMBUCIL-ANTIBODY COMPLEXES.

De Weger RA, Dullens HF, Den Otter W
Dept. Pathology, Utrecht Univ., Pasteurstraat 2, 3511 HX Utrecht, The Netherlands
Immunol Rev; 62:29-45 1982

The use of drug-anti-tumor antibody complexes in which chlorambucil (CL) is non-covalently bound to the antibodies to two mouse tumor systems, the DBA/2-SL2 lymphoma system and the BALB/c Harding Passey melanoma (HPM) system, is reviewed. Immunoglobulin fractions from rabbit-anti-SL2 and -anti-HPM sera were isolated and complexed with CL. DBA/2 mice were injected ip with 2 x 10(5) SL2 cells. Ip treatment of mice with CL-antibody complexes did not prolong the survival of test mice. Of BALB/c mice injected ip with 10(7) HPM cells and treated with five ip injections of CL-antibody complexes, 50% were macroscopically free of tumor 120 days later. Treatment with a mixture of CL and anti-HPM antibody or successive injections of the drug and the antibody (or vice versa) were less successful in the system. When control solutions were tested, the control antibodies as well as CL had some antitumor effect of their own: 10% of the mice treated with one of the components were macroscopically free of tumor 120 days later. Treatment with the immune complex produced significantly better results than treatment with any other solution. (54 Refs)

72. ANTIBODY-INDUCED RELEASE OF CELLULAR PROTEINASES: LOSS OF ADHESION OF HUMAN MELANOMA CELLS AFTER BINDING OF ANTI-MELANOMA ANTIBODY.

Singer KH, Hashimoto K, Stuhlmiller GM, Lazarus GS
Duke Univ. Medical Center, Box 2987, Durham, NC, 22710
J Immunol; 128(3):1321-1326 1982

Incubation of monolayer cultures of human melanoma cells with monkey anti-human melanoma IgG resulted in loss of cellular adhesion. Release of melanoma cells from the culture dish was not the result of cytotoxicity. Antibody-induced cell detachment was partially inhibited by the addition of diisopropylfluorophosphate (DFP), and detachment was completely inhibited by the addition of lima bean trypsin inhibitor. Thiol and carboxyl proteinase inhibitors did not block antibody-induced cellular detachment. An IgG dose-dependent increase in DFP-inhibitable caseinolytic activity was demonstrated in the culture medium of melanoma cells incubated with anti-melanoma IgG, but not in those incubated with normal monkey IgG. Medium collected from antibody-treated cell cultures and incubated with protein A-Sepharose to remove IgG caused detachment of melanoma cells in fresh cultures. Preincubation of this conditioned medium from antibody-treated cell cultures with DFP abolished the medium's ability to mediate loss of cellular adhesion. These data suggest that incubation of melanoma cells with immune IgG results in release of a serine proteinase that mediates cellular detachment. (Author abstract) (36 Refs)

73. ACTIVATION OF FC RECEPTOR-BEARING LYMPHOCYTES BY IMMUNE COMPLEXES. I. STIMULATION OF LYMPHOKINE PRODUCTION BY NONADHERENT HUMAN PERIPHERAL BLOOD LYMPHOCYTES.

Neville ME, Lischner HW

Immunology Lab., St. Christopher's Hosp. for Children, Philadelphia, PA, 19133

J Immunol; 128(3):1063-1069 1982

Activation of human peripheral blood lymphocytes by incubation with particulate immune complexes or aggregated human gamma-globulin was studied by measuring the release of leukocyte migration inhibitory factor (LIF) activity. LIF-active supernatants were consistently produced when nonadherent lymphocytes containing less than 1% surface immunoglobulin-bearing cells and less than 0.2% nonspecific esterase-positive monocytes were incubated in the presence of RBC sensitized with rabbit or human antibodies or with pooled heat-aggregated human gamma-globulin. This immune complex-induced lymphokine production (ICLP) was dependent on the presence of cells bearing receptors for the Fc portion of IgG (Fcgamma). ICLP could not be demonstrated with lymphocyte preparations enriched for B cells even though the latter showed vigorous LIF production in the presence of complement-sensitized erythrocytes. ICLP was dependent on the concentration of lymphocytes and of stimulant as well as on the duration of coincubation, and it required active metabolic processes and RNA and protein synthesis but not DNA synthesis. Ca++ but not Mg++ was obligatory. ICLP by non-B Fcgamma receptor-bearing lymphocytes may play a role in antibody-dependent protective inflammation and immunologic injury phenomena, which is similar to that of lymphokine release by antigen-activated T cells in delayed hypersensitivity responses. (Author abstract) (61 Refs)

74. INVESTIGATION OF CIRCULATING IMMUNE COMPLEXES IN PATIENTS WITH BREAST CANCER.

Horvath M, Fekete B, Raboty P

Natl. Inst. Oncology, P.O. Box 21, 1525 Budapest, Hungary

Oncology; 39(1):20-22 1982

Circulating immune-complex (IC) levels of patients with breast cancer were measured before and after surgery using a complement-consumption technique. Sixteen of 26 patients showed raised pre-operative IC values. In 15 out of 16 patients the pathological IC levels decreased within 2-10 days following surgery. Suggestions about the applicability of this test not only for prognosis, but also for monitoring the course of breast cancer need to be confirmed by further investigations. (Author abstract) (15 Refs)

75. BLOCKADE OF THE HUMORAL IMMUNE RESPONSE: IMMUNE COMPLEXES IN CANCER.

Rosen RD, Morgen AC
Dept. Microbiology and Immunology, Baylor Coll. Medicine, Houston, TX, 77221
The Handbook of Cancer Immunology: Volume 9- Humoral Immunity in Relation to Cancer. Waters H, ed. New York, Garland STPM Press, 289 pp., 1981.

Patients with early stage cancer who show high levels of soluble immune complexes (ICs) in the serum generally have an unfavorable prognosis. The ICs may contain hidden or blocked antibodies reactive against cultured allogeneic tumor cells. The blocking factors may be anti-idiotype antiglobulins or soluble tumor-associated antigens. However, the nature of the ICs in most patients is unknown. Dogs bearing spontaneous tumors were treated by an immunoadsorption technique, in which the plasma was adsorbed with staphylococcal protein A (SPA). This treatment led to marked tumor necrosis, which was attributed to the unblocking of complement-dependent cytotoxic antitumor antibodies hidden within the circulating ICs. A small group of patients with advanced cancers showed similar good responses to immunoadsorption therapy using SPA. Repeated immunoadsorption therapy might eventually lead to the selection of clones of tumor cells which no longer express surface antigens susceptible to attack by unblocked autologous antibodies. Changes in the expression of surface antigens by the tumor cells could also occur as a consequence of repeated immunoadsorption therapy. This treatment will probably have to be combined with chemotherapy, using agents capable of enhancing the tumor cell injury caused by antibody and complement. These encouraging early results lend support to the experimental data suggesting that host responses to autologous tumors are often blocked by circulating factors having many of the properties of soluble antigens or ICs. (168 Refs)

76. RELATIONSHIP BETWEEN CIRCULATING IMMUNE COMPLEXES AND URINARY ANTIGENS IN HUMAN MALIGNANCY.

Huth JF, Gupta RK, Morton DL
Div. Oncology, Dept. Surgery, Univ. California Los Angeles Sch. Medicine, Factor Building, Los Angeles, CA, 90024
Cancer; 49(6):1150-1157 1982

Urine samples obtained from patients with histologically proved melanoma and sarcoma were analyzed for the presence of tumor-associated antigens by complement fixation and enzyme immunoassay. Also, serum samples obtained during 24-hr urine collection from these patients were analyzed for circulating immune complexes by the complement consumption method and by the K562 radiometric assay. Of 36 cancer patients who were positive for urinary antigen (UA) by both assays, 28 (78%) were also positive for CIC in the two assays, 6 (17%) were positive in one of the two CIC-detection assays, and 2 (5%) were negative in both assays. Of 24 patients that were negative for CIC in both assays, 10 (42%) were also negative for UA in both assays, ie, complement fixation and enzyme immunoassay; 12 (50%) were negative by one of the two assays; and only 2 (8%) exhibited UA by both assays. This relationship was more striking for melanoma than sarcoma patients. In a melanoma patient whose samples were studied sequentially during his thermochemotherapy, the fluctuations in CIC and UA were parallel. These results suggest that excretion of tumor-associated antigen into urine is not an isolated phenomenon; rather, immune complex deposition in kidneys appears to cause glomerular damage which may allow the passage of the antigens into the urine. (Author abstract) (32 Refs)

HUMORAL IMMUNOSUPPRESSIVE AGENTS

77. MECHANISMS OF IMMUNOSUPPRESSION IN TUMOR-BEARING MICE: A MULTIFACTORIAL ANALYSIS.

Jessup JM, Kahan BD, Pellis NR
Dept. Surgery, M.D. Anderson Hosp. and Tumor Inst., 6723 Bertner Ave., Houston, TX, 77030
Cancer; 49(6):1158-1167 1982

Neoplastic growth results not only from the inherent proliferative potential of the neoplasm, but also from the neoplasm's ability to survive within a host whose immune responses may be activated to destroy it. It has been proposed that several mechanisms enable a neoplasm to outgrow the host. The present work describes a system for probing tumor-associated immunosuppression by utilization of the delayed hypersensitivity response to dinitrochlorobenzene (DNCB). Mice of the Balb/c and C3H/HeJ strains were sensitized with a subcutaneous injection of 2 mg DNCB followed 5-10 days later by the subcutaneous injection of a 0.05 mg challenge dose of DNCB in the hind footpad. The footpad response measured 24 hr after challenge is a delayed hypersensitivity reaction by virtue of the histology and kinetics of that response and because it is transferred by spleen cells but not by serum. DNCB sensitization is inhibited by spontaneous, chemical - and virus-induced syngeneic tumors in Balb/c an C3H/HeJ mice. Three mechanisms of immunosuppression are elucidated in the present experiments: (1) serum from tumor-bearing mice inhibits primary sensitization of normal mice to DNCB upon passive transfer; (2) spleen cells from tumor-bearing mice inhibit primary sensitization of normal mice to DNCB and appears to be macrophages in the C3H/HeJ system; and (3) an alteration of lymphocyte migration patterns exists in tumor-bearing mice that removes effector cells from the blood and prevents the initiation of a footpad response. The interrelationships of these three mechanisms are discussed. Correlations are also made with tumor-associated immunosuppression observed in cancer patients. (Author abstract) (40 Refs)

78. IMMUNOSUPPRESSION IN NEOPLASIA.

Anderson WL, Tomasi TB
Mayo Medical Sch., Rochester, MN, 55901
The Handbook of Cancer Immunology: Volume 7- Immune Function and Dysfunction in Relation to Cancer. Waters H, ed. New York, Garland STPM Press, 372 pp., 1981.

An immunologic challenge elicits the formation of cells and factors which both enhance and suppress (or terminate) the immune reaction. The net result of the challenge depends on the ratios of these enhancing and inhibitory signals. There is evidence for an association between immunosuppression and neoplasms, but it is not clear whether the immunosuppression is required for tumor establishment (or tumor growth) or a secondary event. Some soluble immunosuppressive factors have been isolated from sera and tumors, but more evidence is needed as to their natures and activities. The possibility that a virus may be responsible for the activity of suppressor cells has not always been excluded. Antigen-specific suppressor T cells are clearly involved in the establishment of tumors. The role of nonspecific suppressor cells is less clear, especially in view of the finding that tumor-bearing animals with elevated levels of nonspecific suppressor cells are not always immunologically comprised. A good correlation has been established between anergy and the presence of soluble immunosuppressive factors (not yet purified) in cancer patients. However, immunosuppression has not been discovered in all or even most cancer patients, and 33% of all cancer patients do not show elevated levels of the immunosuppressive factors which can now be analyzed. These findings suggest that immunosuppression is not a general phenomenon in human cancer and therefore not a requirement for tumor development. However, it is possible that immunosuppressive elements may act locally at the tumor site. Currently used tests of immune function may not detect subtle but important abnormalities. Future research should provide both a better understanding of both immune regulation in neoplasia and normal immune homeostatic mechanisms. (124 Refs)

79. TUMOR ASSOCIATED IMMUNOSUPPRESSIVE SERUM PROTEINS.

Ninnemann JL
Dept. Surgery, Sch. Medicine, Univ. California, San Diego, CA, 92037
The Handbook of Cancer Immunology: Volume 8- Tumor Antigens: Structure and Function. Waters H, ed. New York, STPM Garland Press, 418 pp., 1981.

A tumor-associated immunosuppressive factor (ISF) or complex of factors was isolated from the sera of patients who had been treated only by surgery for advanced melanomas (Clark's Level IV-V) up to 2 yr previously. Serum ISF levels were significantly elevated in 7/14 patients; 3/7 later died, and 2/7 others showed marked increases in serum ISF activity as their tumors spread. The other 7/14 patients were all alive at the time of report. The immunosuppressive effects (in vitro) of preoperative sera were often inhibited by non-immunosuppressive autologous sera obtained 2-3 wk postoperatively. Anti-immunosuppressive antibodies were found in the non-immunosuppressive sera. Preliminary analytical studies identified this ISF as an immunogenic substance; probably a protein; probably of high mol wt; extremely stable to heat but inactivated by prolonged freezing or repeated freeze-thawing; unrelated to RNA, DNA, or cortisol; not an immunoglobulin (Ig); and not alpha-2-macroglobulin (A2MG) although possibly associated with A2MG. This ISF may be only one of many tumor-associated immunosuppressive factors recoverable from the sera of patients with advanced cancer (Ig, immune complexes, alpha-globulin, prostaglandins, carcinoembryonic antigen, and histamine are reportedly involved). However, there are several possible sources of misleading information in the search for immunosuppressive tumor-associated serum components, which are discussed. (120 Refs)

OTHER RELATED STUDIES

80. EFFECT OF MOUSE HEPATITIS VIRUS INFECTION ON 'NATURAL KILLER CELL' ACTIVITY IN NUDE MICE.

Tamura T, Sakaguchi A, Ishida T, Fujiwara K
Dept. Animal Pathology, Inst. Medical Science, Univ. Tokyo, Shirokanedai, Minato-ku, Tokyo 108, Japan
Microbiol Immunol; 25(12):1363-1368 1981

The effects of the NuU strain of mouse hepatitis virus (MHV) on natural kill (NK) cells was studied in male nude (nu/nu) and female heterozygous (nu/+) mice with a BALB/c background. NK cell activity of spleens from MHV-infected nu/nu and nu/+ mice was determined in microtiter wells with 10(4) radio-labeled cells of different established cell lines (DBT, L-929, RL male-1 [RL], or YAC-1). The cytotoxicity of spleen cells from nu/+ against Yac-1 and RL cells was markedly elevated at 1 and 4 days after ip infection with MHV-Nu, and decreased thereafter. In nu/nu cells, significant toxicity against DBT cells was seen only 1 day after infection and activity was low at 4 days or later. No cytotoxicity was found in either nu/nu or nu/+ cells. Since NK activity seemed to be enhanced after MHV infection in both nu/nu and nu /+ cells, the effective cell population was determined with spleen cells from nu/nu mice 24 hr after infection with MHV. Spleen cells passed through Sephadex G-10 showed high cytotoxicity for all target cells comparable to that of whole preparations. Depletion of B cells significantly increased toxicity, while that of adherent cells was low. Titers of 1:1,000 to 1:2,000 of interferon (IFN) were detected until 2 days after infection in both nu/nu and nu/+ mice. In another study, nu/nu mice were injected ip with either UV-irradiated nu/+ spleen homogenate having an IFN titer of 1:800, or with UV-inactivated MHV, and spleen cells were examined for NK activity 24 hr later. Neither the transfer of infected nu/+ spleen homogenate nor the injection of UV-inactivated MHV affected NK activity. The NK activity increased throughout the course of MHV infection, but transferred IFN had no effect on NK activity. (19 Refs)

81. IMMUNOTOXINS: HYBRID MOLECULES COMBINING HIGH SPECIFICITY AND POTENT CYTOTOXICITY.

Jansen FK, Blythman HE, Carriere D, Casellas P, Gros O, Gros P, Laurent JC, Paolucci F, Pau B, Poncelet P, Richer G, Vidal H, Voisin GA

Centre de Recherches Clin-Midy, 34082 Montpellier, France

Immunol Rev; 62:185-216 1982

Experience with four different immunotoxin (IT) models is used as a basis for review of the high specific activity of conjugates between antibodies and the A-chain of ricin, the essential requirements for optimal in vitro IT activity, and advantages and limitations of IT in vitro and in vivo. The three subunits of IT, the toxin, the antibody, and the chemical linkage, are described. After presentation of the cellular model, in vitro and in vivo IT activities are demonstrated. Some conditions necessary to compare ITs of different origin and the possible applications of IT are listed. In vitro properties (sensitivity of different cell lines to toxin, ultrastructural lesions resulting from ricin activity) and in vivo properties (general toxicity, histopathological alterations) of ricin and ricin A-chains are described. Labile, stable, and long spacer disulfide bridges are considered. Cellular models are described for artificial antigens, and mouse differentiation, human differentiation, and human tumor-associated antigens. Advantages of IT include immunological specificity, high efficiency, potentiation, stability, and reproducibility. Essential requirements for high IT efficiency include high purification A-chain, nondenaturing labile disulfide bridge, high affinity of purified antibodies, and potentiation of IT activity, Limitations of IT include relative cellular resistance, slow kinetics, and dependence on in vitro conditions. In vivo findings on IT physiopathology (lethal doses, in vivo half-life, nonspecific toxicity, immunogenicity) and tumor growth inhibition are reported. (55 Refs)

82. HUMAN MONOCLONAL AUTOIMMUNE ANTIBODY PRODUCED IN VITRO: RHEUMATOID FACTOR GENERATED BY EPSTEIN-BARR VIRUS-TRANSFORMED CELL LINE.

Steinitz M, Tamir S
Dept. Hematology, Hadassah Univ. Hosp., Kiryat Hadassah, P.O. Box 12 000, IL-91 120, Jerusalem, Israel
Eur J Immunol; 12(2):126-133 1982

The infection of selected lymphocytes from a rheumatoid arthritis patient with Epstein-Barr virus resulted in an immortalized cell line that secretes a monoclonal rheumatoid factor (RF). The cloned line has been growing for more than 24 mo, and constantly produces a monoclonal IgM,lambda, 19S, RF (1-2 ug/ml/10(6) cells). The RF agglutinates human and rabbit IgG (but not IgM) and also protein A-coated erythrocytes, but fails to do so to mouse, goat and swine IgG-coated erythrocytes. When bound to immune complexes, this monoclonal RF does not bind complement. In the cell supernatant RF is the only immunoglobulin and it comprises approx 5% of the total proteins. The affinity of RF to aggregated human IgG, as detected in inhibition experiments, is higher than that of Fc receptors found on human non-T lymphocytes, K562 and Daudi cell lines. (Author abstract) (44 Refs)

83. METHOD DEVELOPED FOR RADIOSENSITIVITY EXAMINATION OF T-HELPER CELLS.

Temesi A, Pellet S
'Frederic Joliot-Curie' Natl. Res. Inst. Radiobiology and Radiohygiene, P. O. Box 101, H-1775 Budapest, Hungary
Stud Biophys; 86(1):79-80 1981

Deterioration of radiosensitivity of T-helper cells was studied in vivo in BD2F1 hybrid mice injected with thymus and sheep erythrocytes after 850 R Co-60 gamma-irradiation. Antibody forming ability of spleen cells was measured. Different subpopulations of T-cells manifested helper and suppressor function. Results showed that suppressor function of T-cells following 150-250 rad decreases to such an extent that function activity of T-helper cells is increased. Following 450 rad irradiation, injury of T-helper cells was observed. (3 Refs)

84. PREVENTION OF THE IN VITRO MYELOSUPPRESSIVE EFFECTS OF GLUCOCORTICOSTEROIDS BY INTERLEUKIN 1 (IL 1).

Mishell RI, Lee DA, Grabstein KH, Lachman LB
Dept. Microbiology and Immunology, Univ. California, Berkeley, CA, 94720
J Immunol; 128(4):1614-1619 1982

We investigated the effects of dexamethasone on the formation of granulocyte/macrophage colonies by murine bone marrow cells cultured with colony-stimulatory factors (CSF) in semisolid agar. Dexamethasone (10-7M) completely inhibited the formation of colonies in response to L929 CSF but had no effect on the response to CSF in the culture supernatants of the murine macrophage cell line, PU5-1.8. We postulated that a cofactor, interleukin 1, present in the PU5-1.8 supernatants was responsible for protecting colony formation against steroid suppression. Interleukin 1, isolated from culture supernatants of PU5-1. 8 and from culture supernatants of human acute monocytic leukemia cells, blocked the inhibitory effects of dexamethasone on colony formation in response to L929 CSF. Moreover, dexamethasone inhibited colony formation in response to PU5-1.8 culture supernatants when interleukin 1 was absent. We also examined interleukin 2 for possible protective effects. Although crude interleukin 2 preparations (supernatants of spleen cells cultured with concanavalin A) blocked dexamethasone inhibition, purified interleukin 2 had no protective effects. These data indicate that interleukin 1 protects colony formation by a pathway that is independent of interleukin 2 and that supernatants of spleen cells activated with concanavalin A probably contain significant amounts of interleukin 1. (Author abstract) (64 Refs)

85. REACTIVITY OF MONOCLONAL ANTIBODIES AGAINST HUMAN LEUCOCYTE ANTIGENS WITH LYMPHOCYTES OF NON-HUMAN PRIMATE ORIGIN.

Neubauer RH, Levy R, Strnad BC, Rabin H
Biological Carcinogenesis Program, Frederick Cancer Res. Center, P.O. Box B, Frederick, MD, 21701
J Immunogenet; 8(6):433-442 1981

A series of B- and T-lymphoid cells of human and nonhuman primates (gorilla, chimpanzee, orangutan, gibbon, baboon, owl monkey, marmoset) and fresh peripheral blood lymphocytes were used to examine phylogenetic distributions of the antigens present on human lymphocytes. These antigens were identified with murine monoclonal antibodies specific for a T-cell antigen, lymphoid and lymphoid:myeloid antigens, Ia antigens, and beta 2 microglobulin. Reactivity of the monoclonal antibodies was detected using anti-murine IgG reagent. Monoclonal antibodies directed against human leukocyte antigens react with other primate species in a pattern consistent with known phylogenetic relationships. Human antigenic determinants were restricted to the great apes (gorilla, chimpanzee) whereas the Ia antigens reacted with cells of both Old and New World primate species. Immunoprecipitation analyses using 125I-labeled B-cell lines analyzed following sodium dodecyl sulfate polyacrylamide gel electrophoresis demonstrated that the molecular structures of the Ia antigens differ not only between human cells and cells of lower primates, but between those on owl monkey and marmoset cells. (35 Refs)

86. RELATIONSHIP OF CELL-CYCLE EXPRESSION OF IA-LIKE ANTIGENIC DETERMINANTS ON NORMAL AND LEUKEMIA HUMAN GRANULOCYTE-MACROPHAGE PROGENITOR CELLS TO REGULATION IN VITRO BY ACIDIC ISOFERRITINS.

Broxmeyer HE
Dept. Developmental Hematopoiesis, Sloan-Kettering Inst. Cancer Res., New York, NY, 10021
J Clin Invest; 69(3):632-642 1982

An association has been established between human Ia-like (Ia) antigenic determinants, expression during DNA synthesis on granulocyte-macrophage colony forming cells (CFU-GM) and the regula tory action of acidic isoferritins in vitro. Treatment of human bone marrow cells with monoclonal-anti-Ia-like (Ia) plus complement inhibited colony and cluster formation by approx 50% but did not affect pre-CFU-GM. Reduction of colonies and clusters was similar whether bone marrow cells were exposed to anti-Ia plus complement, high specific activity tritiated thymidine (3HTdr) or acidic isoferritins. No further decrease was apparent with 3HTdr or acidic isoferritins after Ia-antigen+ CFU-GM were removed, or with anti-Ia plus complement or acidic isoferritins after DNA synthetic phase (S-phase) CFU-GM were removed. Anti-Ia, without complement, did not reduce colony or cluster formation but did block the inhibitory action of acidic isoferritins. A relationship existed between Ia antigens and the activity of acidic isoferritins in the following ways: (a) The apparent loss of Ia-antigens from CFU-GM by 5 hr in culture at 37 C, but not at 27 C or 4 C, was associated with nonresponsiveness to inhibition with acidic isoferritins, (b) Ia-antigen-, noncycling pre-CFU-GM that were insensitive to acidic isoferritins could generate a population of Ia-antigen+ cycling CFU-GM in vitro that were responsive to inhibition by acidic isoferritins, and (c) nondetectability of Ia-antigens on CFU-GM from patients with leukemia was associated with nonresponsiveness to inhibition by acidic isoferritins. These results implicate Ia-antigen+ progenitor cells in the regulation of myelopoiesis in vitro and demonstrate that absence of Ia-antigens on patient CFU-GM is associated with imbalances in normal regulatory interactions in vitro. These findings may be of relevance to normal regulation and to the progression of leukemia. (Author abstract) (30 Refs)

87. CELLS BEARING FC RECEPTORS IN HUMAN MALIGNANT SOLID TUMOURS.

Svennevig JL, Andersson TR
Dept. Surgery, Rikshospitalet, Oslo, Norway
Br J Cancer; 45(2):201-208 1982

Fc-receptor-bearing cells forming EA rosettes with antibody-coated human erythrocytes (Ripley) were studied in cell suspensions and in purified preparations of mononuclear cells (MC) from 20 human malignant tumors. The EA rosettes were studied in preparations made by cytocentrifugation and the rosette-forming cells identified by their nonspecific-esterase activity and phagocytic capacity. Fc receptors were found on 16 +-20% of all cells in the primary cell suspensions. Significantly more tumor-infiltrating lymphocytes had detectable Fc receptors (33 +-18%) than did peripheral-blood lymphocytes in cancer patients (19 +-8%) and normal control subjects (14 +-6%). There was a significant correlation between the proportion of lymphocytes lacking T and B markers (null cells) and the proportion of lymphocytes with Fc receptors. Fc receptors were also found on most tumor-infiltrating macrophages, on some T lymphocytes and pol ymorphonuclear cells and on a smaller percentage of the tumor cells. The significance of the Fc receptor and its usefulness as a marker of 'host infiltration' into the tumors is discussed. (Author abstract) (29 Refs)

88. ANALYSIS OF NATURAL KILLER ACTIVITY AND ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY IN HEALTHY VOLUNTEERS AND IN PATIENTS WITH PRIMARY LUNG CANCER AND METASTATIC PULMONARY TUMORS.

Saijo N, Shimizu E, Irimajiri N, Ozaki A, Kimura K, Takizawa T, Niitani H
Dept. Internal Medicine, Natl. Cancer Center Hosp., Tsukiji 5-1-1, Chuo-Ku, Tokyo 104, Japan
J Cancer Res Clin Oncol; 102(3):195-214 1982

To clarify the contribution of ADCC and NK activities to host immune response against cancer, the characteristics of cells mediating these activities were examined in the peripheral blood lymphocytes of normal volunteers, and the changes of these activities were also evaluated in patients with lung cancer and metastatic pulmonary tumors before and after chemotherapy. OAT cells derived from small cell carcinoma of the lung and K-562 cells derived from erythroleukemia were used as target cells of ADCC and/or NK assay. ADCC and NK activities were not changed according to age, sex, and blood type. Mild and marked personal differences were observed in ADCC and NK activity, respectively. These activities were also influenced by environment. ADCC and NK activities of normal adult volunteers were diversely correlated at the coefficient of gamma-0.426. NK activities were high against K-562 and CCRF-CEM cells, and low against BALL and OAT cells. NK activity against K-562 cells was strongly inhibited by K-562 or CCRF-CEM cells with high NK sensitivity, on the other hand, it was slightly inhibited by OAT and BALL cells with low NK sensitivity. NK activity against OAT cells was strongly inhibited by OAT, K-562 and CCRF-CEM cells, but not inhibited by BALL cells. The effector cells mediating NK activity were identified as non-adherent, E-receptor-positive, Fc-receptor-positive small lymphocytes. NK activity was not decreased before chemotherapy in patients with stage III primary lung cancer and metastatic pulmonary tumors. It was decreased only in patients of bad performance status, and it was significantly decreased in all patients after chemotherapy. ADCC also exhibited the tendency to decrease after chemotherapy in tumor-bearing patients. The recovery of NK-activity after chemotherapy well correlated with the effect of chemotherapy. (Author abstract) (53 Refs)

89. INDUCTION OF T15-SPECIFIC SUPPRESSOR T CELLS IN MICE WITH THE CBA/N DEFECT BY NEONATAL INJECTION WITH ANTI-T15 IDIOTYPE ANTIBODY.

Kim BS, Massey PB
Dept. Microbiology-Immunology, Northwestern Univ., Chicago, IL, 60611
J Immunol; 128(3):1145-1148 1982

Mice with the CBA/N defect (xid) are unresponsive to phosphorylcholine (PC). To determine whether idiotype-specific suppressor T cells can also be generated in these defective mice, defective (CBA/N x BALB/c)F1 male and nondefective (CBA/N x BALB/c)F1 female or (BALB/c x CBA/N)F1 male mice were neonatally injected with antibodies specific for the major idiotype of anti-PC antibody, ie, anti-TEPC-15 idiotype (T15id) antibody. Suppressor cell activity was examined by co-culturing spleen cells from neonatally treated F1 mice with spleen cells of normal nondefective F1 mice in the presence of antigen. Spleen cells from defective (CBA/N x BALB/c)F1 mice treated with anti-T15id antibody demonstrated a level of suppressor activity (greater than 83% suppression) comparable to that of similarly treated nondefective F1 mice. This suppression was specific for the T15id of anti-PC response, and a Lyt-1(-)2+-bearing T cell population appeared to be responsible for the active suppression. These suppressor T cells recognized T15 but not PC, based on a functional absorption test. These results indicate that the CBA/N defects, including the deficiency in the anti-PC response by B lymphocytes and a possible T cell defect, do not influence the generation of T15id-specific suppressor T cells by neonatal injection with anti-T15id antibody. (Author abstract) (33 Refs)

90. STUDIES ON THE MECHANISMS OF THE INHIBITORY EFFECTS OF SERUM THYMIC FACTOR ON MURINE ALLOGRAFT IMMUNITY.

Kaiserlian D, Dardenne M
Inserum U 25, Hopital Necker, 161, rue de Sevres, 75015 Paris, France
Cell Immunol; 66(2):360-371 1982

The mechanisms of the inhibitory effect of the serum thymic factor (FTS) on allograft immunity have been studied on both cellular and humoral immune responses of skin allografted mice. FTS-induced suppression of allogeneic skin graft rejection was correlated with a transient diminution of in vivo alloreactive CTL production in the spleen, whereas the generation of allo-anti-H-2 antibodies was not affected. The involvement of suppressor cells in the effect of FTS was supported by the observation that irradiated spleen cells from FTS-treated recipients (bearing a 9-day allograft) suppressed the in vitro CTL generation. (Author abstract) (29 Refs)

91. A GENERAL METHOD FOR THE CYTOCHEMICAL AND ULTRASTRUCTURAL STUDIES OF HUMAN LYMPHOCYTE SUBSETS DEFINED BY MONOCLONAL ANTIBODIES.

Bernard J, Ternynck T, Zagury D
Institut Jean-Godinot, 51100 Reims, France
Immunol Lett; 4(2):65-73 1982

A method of general applicability is described for further characterization of lymphocyte subsets as defined by monoclonal antibodies. Human lymphocyte subpopulations were identified by means of anti-mouse immunoglobulin (Ig)-coated latex microspheres or ox RBC following treatment with mouse hybridoma antisera specific for differentiation markers on the surface of T- or B-cells. Optimal conditions are described for a panel of monoclonal mouse hybridoma antisera from various sources. The method is as sensitive as the complement-mediated microcytotoxicity assay, is rapid, easy to perform and permits exhaustive light and electron microscopic studies of lymphocytes bound to the carrier particles. Correlation between membrane differentiation antigens detected by monoclonal antibodies and intracellular enzyme markers established by cytochemical treatment of rosettes can provide additional data on the association of membrane and cytoplasmic lymphocyte markers and possibly reveal discrete stages of lymphoid cell maturation and provide information on the classification of neoplastic lymphocytes. (18 Refs)

92. IMMUNOREGULATION OF MURINE MYELOMA IN VITRO. II. SUPPRESSION OF MOPC-315 IMMUNOGLOBULIN SECRETION AND SYNTHESIS BY IDIOTYPE-SPECIFIC SUPPRESSOR T CELLS.

Milburn GL, Lynch RG
(c/o Lynch) Dept. Pathology, Univ. Iowa Coll. Medicine, Iowa City, IA, 52242
J Exp Med; 155(3):852-862 1982

The 2,4,6-trinitrophenyl (TNP)-specific BALB/c plasmacytoma MOPC-315 was studied; MOPC-315 is a monoclonal B cell population responsive to idiotype-specific and TNP-antigen-specific immunoregulatory signals. An in vitro system was used to examine the mechanism of inhibition of IgA anti-TNP antibody (M315) secretion, mediated by the idiotypic antigens located in the variable regions of M315 produced by MOPC-315. Inhibition of M315 secretion by Id315-specific suppressor T cells is mediated by a Lyt-2+ cell that expresses a surface membrane receptor for Id315. The suppressor signal is a diffusable product that acts directly on M315-secreting myeloma cells. Inhibition of M315 secretion is T cell dose-dependent, Id315-specific, reversible, and results from inhibition of M315 synthesis, as demonstrated by inhibition of (3H)leucine incorporation into MOPC-315. Suppressor T cells can act directly on B cells as late in B cell development as the actual antibody-secreting cell. Although the precise molecular mechanism for selective inhibition of M315 synthesis is unknown, it is likely achieved at the level of transcription or translation. (25 Refs)

93. DISORDERS OF HUMAN LEUKOCYTE CHEMOTAXIS.

Lohr KM, Snyderman R
Div. Rheumatology, Medical Coll. Wisconsin, 8700 Wisonsin Ave., Milwaukee, WI, 53226
Clin Immunol Rev; 1(1):67-118 1981

Mechanisms and disorders of WBC motility are reviewed. Chemotactic factors and assays of WBC motility are described. Disorders of WBC include intrinsic defects (transient or persistent polymorphonuclear WBC disorders), defective production of chemotactic factors (abnormalities of immunoglobulins, complement, or coagulation factors), humoral inactivators of chemotactic factors (abnormal levels of naturally-occurring inactivators, acquired inactivators), and cell-direct inhibitors of WBC chemotax is (abnormal levels of naturally-occurring inhibitors, acquired inhibitors). Disorders of WBC motility can lead to increased susceptibility to infections, inflammatory disorders, or neoplastic diseases. (249 Refs)

94. DEPLETION OF LYMPHOCYTE SUBPOPULATIONS IN PRIMARY AND SECONDARY LYMPHOID ORGANS OF MICE BY A TRANSPLANTED GRANULOCYTOSIS-INDUCING MAMMARY CARCINOMA.

Lee MY, Rosse C
Div. Hematology, Dept. Medicine RM-10, Univ. Washington Sch. Medicine, Seattle, WA, 98195
Cancer Res; 42(4):1255-1260 1982

Transplanted CE mammary carcinoma causes a marked increase in the production of neutrophilic granulocytes in mice associated with the expansion of hemopoietic marrow into the peripheral skeleton. Changes in lymphocyte populations in the femoral marrow, the expanding peripheral marrow, and the spleen were examined for a period of 3 wk post-tumor transplantation using fluoresceinated antisera specific for B- and T-cells. As tumor growth and granulocytic hyperplasia progressed, B- and T-cells became reduced in femoral marrow and the spleen, but lymphocytes of undefined function, devoid of T- and B-cell surface antigens (null cells), transiently increased in femoral marrow and in the spleen. In the expanding peripheral marrow, such null cells increased and remained as the predominant cell type until granulocytic hyperplasia took place. These changes suggest shifts in the site of myelogenous lymphocyte production or in the differentiation program of lymphocytes. The thymus invariably showed marked atrophy which, as shown in adrenalectomized animals, could not be explained entirely by tumor-induced stress. Thus, the massive granulocytopoietic effects of CE mammary carcinoma are coupled with marked changes in lymphocyte populations due, most likely, to the tumor's influence on primary lymphoid organs. (Author abstract) (26 Refs)

95. GENERATION OF A MONOCLONAL ANTIBODY AGAINST FACTEUR THYMIQUE SERIQUE (FTS).

Ohga K, Incefy GS, Wang CY, Good RA
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Clin Exp Immunol; 47(3):725-734 1982

A monoclonal antibody against one of the thymic hormones, facteur thymique serique (FTS), was generated by hybridization between mouse NS-1 myeloma cells and BALB/c splenocytes, the latter obtained from BALB/c mice immunized with synthetic FTS coupled to mouse IgG. Enzyme-linked immunosorbent assay (ELISA) was developed and employed to detect the hybridoma secreting specific antibody. The monoclonal

antibody (MA-FTS) was highly specific for FTS and did not cross-react with other thymic hormones or other unrelated peptides. MA-FTS could recognize FTS (or FTS-like molecule) in human serum and could absorb completely the FTS-like activity from human serum. (Author abstract) (25 Refs)

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TUMOR ANTIBODY PRODUCTION/ CHARACTERIZATION/ DETECTION

1. CHARACTERIZATION OF A MONOCLONAL ANTIBODY REACTIVE WITH A SUBSET OF HUMAN BREAST TUMORS.

Yuan D, Hendler FJ, Vitetta ES
(c/o Hendler) Dept. Internal Medicine, Univ. Texas Health Science Center at Dallas, 5323 Harry Hines Blvd., Dallas, TX, 75235

JNCI; 68(5):719-728 1982

Fusion of spleen cells, from mice immunized against the human hormone-dependent breast cancer cell line ZR-75-1,

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C.B. 08/83/87

with murine myeloma cells resulted in the establishment of a hybridoma cell line, HY59-H10(H59). The purified monoclonal IgM produced by the hybridoma reacts with the most differentiated human breast tumor cell lines but not with cells derived from normal breast secretions or with numerous other malignant cell lines. Of 106 biopsy specimens examined, H59 bound to 54% of malignant breast specimens, to 83% of fibroadenomas, and to 82% of specimens containing fibrocystic disease. Binding could not be detected in uninvolved breast tissue. (Author abstract) (52 Refs)

2. A MONOCLONAL ANTIBODY TO AN INTERSPECIES MAJOR HISTOCOMPATIBILITY DETERMINANT INHIBITS A VIRUS-SPECIFIC T-CELL CLONE.

Allouche M, Bennink JR, McKearn TJ, Doherty PC
(c/o Doherty), Wistar Inst. Anatomy and Biology, 36th St. at Spruce, Philadelphia, PA, 19104
Cell Immunol; 68(1):193-198 1982

The cytotoxicity of an influenza-specific T-cell clone of BALB/c mouse origin for an H-2 compatible, virus-infected target is greatly inhibited by a monoclonal antibody which binds to mouse major histocompatibility complex (MHC) determinants, but was originally prepared against MHC antigens of the Brown Norway (BN) rat. The inhibition is still observed after absorption of the antibody with lymphoid cells from Lewis, but not from BN or Lewis 1N rats. It thus seems that the site blocked by this monoclonal antibody, which interacts with MHC antigens from a number of animal species, is at least close to a determinant on the MHC glycoprotein that is involved in T-cell recognition. This reagent may be useful for comparative analysis of the phylogeny of MHC-restricted T-cell responses in different species. (Author abstract) (18 Refs)

3. HUMAN-MOUSE HYBRIDOMA CELLS PRODUCING ANTIBODIES.

Astaldi GC, Willems C, Alleyne W, Lansdorp P, Zeijlemaker WP, Janssen M
Central Lab., Netherlands Red Cross Blood Transfusion Service, Amsterdam, The Netherlands
Protides Biol Fluid Proc Colloq; 29:609-614 1982

Xenogeneic hybridomas between human lymphocytes and mouse myeloma cells were produced and the effects of various factors on their growth were studied. After fusion, cells were resuspended in culture medium containing 10% human endothelial culture supernatant (HECS) and when hybrid clones developed, the supernatants were tested for the presence of antibodies against RhD+ RBC. The hybridoma cells producing anti-D activity were expanded and cloned by limiting dilution in culture medium containing 10% HECS. Six days of culture in the presence of pokeweed mitogen strongly increased the yield of hybridoma cells. The recovery of hybridoma cells producing anti-D antibodies was significantly increased by culturing the lymphocytes in the presence of RhD+ RBC together with endothelial cells. All eight hybridoma supernatants agglutinating RhD+ RBC had specificity for the D antigen. Specific antibody production decreased markedly with time, indicating the instability of the xenogeneic hybridoma cells. Selection for antibody-producing clones was accomplished by culturing at low density and discarding negative clones. The percentage of wells containing hybridoma cells producing anti-D antibodies increased upon each passage up to the fourth passage, when a plateau was reached. Thus, when lymphocytes obtained from persons who had been immunized with allogeneic RhD+ RBC were fused with mouse myeloma cells, hybridoma cells were obtained producing specific anti-D antibodies. (13 Refs)

4. CHARACTERISATION OF MONOCLONAL ANTIBODIES TO CARCINOEMBRYONIC ANTIGEN BY ANTIBODY OVERLAY OF POLYACRYLAMIDE SLAB GELS.

Chester KA, Begent RH
Dept. Medical Oncology, Charing Cross Hosp., London W6 8RF, England
Protides Biol Fluid Proc Colloq; 29:911-914 1982

Two monoclonal antibodies (MS1 and MS200) taken from BALB/c mice bearing myeloma cells in ascites form were produced against carcinoembryonic antigen (CEA) and their binding characteristics studied. CEA samples from different sources were subjected to sodium dodecyl sulfate polyacrylamide slab gel electrophoresis (SDS PAGE) and the separated tracks were overlaid with serum from MS1, MS200 or normal mice. Binding of the monoclonal antibodies to components of different mol wt was demonstrated by autoradiography after overlay with 125I-labeled antibody directed against mouse IgG. Different binding patterns were observed with different antibodies in the same CEA preparation and with the same antibody in different CEA preparations. The epitope with which MS200 reacted seemed to be expressed more often on the lower mol wt component than the higher component, while that reacting with MS1 was equally represented on both peaks. Thus, MS1 and MS200 have different binding characteristics to the same CEA preparation, and the two antibodies are specific for different epitopes. The value of this technique for characterization of monoclonal antibodies and protein antigens is evident. (4 Refs)

5. MONOCLONAL ANTIBODIES AGAINST CARCINOEMBRYONIC ANTIGEN.

Hedin A, Hammarstrom S
Dept. Immunology, Univ. Stockholm, Stockholm, Sweden
Protides Biol Fluid Proc Colloq; 29:907-910 1982

Monoclonal antibodies against carcinoembryonic antigen (CEA) were produced using a hybridoma technique. Spleen cells from BALB/c mice immunized with highly purified CEA were fused with mouse myeloma cell line Sp2/0-Ag 14. Data on eight monoclonal antibodies against CEA obtained from cells cultured for 4 mo are reported. All eight antibodies were IgG 1 and six showed different isoelectric points. Three different titration curves of supernatant reactivity were seen. Six of the eight antibodies were directed against conformation dependent epitopes on the CEA molecule since they showed a marked decrease in reactivity against reduced and alkylated CEA as compared to the native molecule. All antibodies showed approx equal reactivity against Smith degraded CEA compared to native CEA. It was concluded that the antibodies were directed against the protein moiety of the molecule. One antibody gave a precipitate when tested in immunodiffusion against CEA; however, when two different antibodies were combined and tested against CEA, strong precipitates were seen in several combinations. Thus, at least five antibodies recognize different epitopes on the CEA molecule. (6 Refs)

HE 20.3173/2:

6. PREPARATION AND CHARACTERIZATION OF MONOCLONAL ANTIBODIES AGAINST ANTIGENS OF HUMAN RENAL ADENOCARCINOMA.

Hess H, Alheid U, Biermann S, Waks T, Scherberich JE, Mondorf AW, Schoeppe W, Senge T, Falkenberg FW
Dept. Nephrology, Center for Internal Medicine, Klinikum J. W. Goethe Universitat, 6000 Frankfurt am Main, W. Germany
Protides Biol Fluid Proc Colloq; 29:903-905 1982

Lymphocytes from BALB/c mice hyperimmunized by four and eight consecutive injections of renal adenocarcinoma plasma membranes were fused with X63-Ag 8.653 plasmacytoma cells. In the supernatants of 90/600 wells with viable cells, antibodies reactive with antigens in tumor and/or kidney were found. Twenty-two clones were isolated and characterized. Tumor cell membranes, capillaries and intercellular matrix were recognized by the various monoclonal antibodies. Generally, the density of antigenic determinants was higher in the tumor than in normal kidney tissue. No monoclonal antibodies were found that reacted exclusively with tumor. Localization of antigenic determinants in the kidney was easy, while in the tumor tissue localization could not be defined exactly. Antibodies of Hyp I 164 D5 and Hyp I 289 A1 reacted with tumor cell membranes, antibody Hyp I 238 A9 with capillaries. (5 Refs)

TUMOR ANTIBODIES ASSOCIATED WITH VIRUSES

7. MONOCLONAL ANTIBODIES TO EPSTEIN-BARR VIRUS-INDUCED, TRANSFORMATION-ASSOCIATED CELL SURFACE ANTIGENS: BINDING PATTERNS AND EFFECT UPON VIRUS-SPECIFIC T-CELL CYTOTOXICITY.

Rowe M, Hildreth JE, Rickinson AB, Epstein MA
Dept. Pathology, Univ. Bristol Medical Sch., University Walk, Bristol BS8 1TD, England
Int J Cancer; 29(4):373-381 1982

Spleen cells from mice immunized with Epstein-Barr virus-transformed lymphoblastoid cells (EB-LCL) were used to generate monoclonal antibodies to cell surface antigens associated with the EB virus-transformed state. Radioimmune and immunofluorescence binding assays identified two antibodies, MHM6 and AC2, which reacted consistently with all EB-LCL tested, with a subpopulation of cells in some but not all EB virus genome-positive Burkitt lymphoma lines, but with none of a range of EB virus genome-negative cell lines of lymphoma or leukemia origin. While MHM6 appeared to bind an EB virus-related antigen, AC2 bound some other cell surface antigen which was also found on a small subpopulation of cells in lymphocyte cultures stimulated with phytohemagglutinin or with pokeweed mitogen. MHM6 and AC2 recognized single polypeptides with apparent mol wt of 45 kd and 80 kd respectively as shown by sodium dodecylsulphate polyacrylamide gel electrophoresis (SDS-PAGE) analysis of 125I-labeled cell surface polypeptides immunoprecipitated with these antibodies. These polypeptides were induced on experimentally-infected B cells within 24 hr of the expression of the EB virus nuclear antigen, EBNA, at a time known to coincide with the appearance of the lymphocyte-detected membrane antigen, LYDMA. However, saturating concentrations of MHM6 and of AC2 were unable to protect EB-LCL target cells from lysis by LYDMA-specific cytotoxic T cells in a chromium-release assay. (Author abstract) (50 Refs)

8. MEMBRANE ANTIGEN ON EPSTEIN-BARR VIRUS-INFECTED HUMAN B CELLS RECOGNIZED BY A MONOCLONAL ANTIBODY.

Slovin SF, Frisman DM, Tsoukas CD, Royston I, Baird SM, Wormsley SB, Carson DA, Vaughan JH
(c/o Vsughan) Dept. Clinical Res., Scripps Clinic and Res. Foundation, La Jolla, CA, 92037
Proc Natl Acad Sci USA; 79(8,part1):2649-2653 1982

This paper describes a monoclonal antibody (B532) that detects a membrane antigen present on greater than or equal to 95% of the B cells from lines carrying the Epstein-Barr virus (EBV) genome. Evidence suggesting that B532 is EBV-related was originally obtained by using a cell-binding radioassay with different cell line substrates. Immunofluorescence and cell-sorter analysis confirmed that the antigen was present in high density on all EBV-infected lymphoblastoid B-cell lines, but not on EBV-negative B-, T-, myeloid, or null cell lines. Isolated normal peripheral blood B and T lymphocytes and monocytes failed to bind B532. The monoclonal antibody did not inhibit in vitro EBV infection nor did it block the killing of EBV-infected targets by cytotoxic T lymphocytes. The cell surface antigen recognized by B532 was shown by immunoprecipitation to have a mol wt of approx 45,000. (Author abstract) (38 Refs)

9. PROPERTIES OF MOUSE LEUKEMIA VIRUSES. XVIII. EFFECTIVE TREATMENT OF AKR LEUKEMIA WITH ANTIBODY TO GP71 ELIMINATES THE NEONATAL BURST OF ECOTROPIC AKR VIRUS PRODUCING CELLS.

Fischinger PJ, Dunlop NM, Schwarz H, Ihle JN, Weinhold K, Bolognesi DP, Schafer W
Virus Control Section, NCI, Frederick, MD, 21701
Virology; 119(1):68-81 1982

To suppress spontaneous leukemia, treatment of AKR mice with antibody to the murine leukemia virus (MuLV) major glycoprotein (gp71) must commence during a narrow 'window' period between birth and Day 3. To examine the effect of treatment on virus expression, infectious MuLV cell centers (ICCs), free MuLV, and viral antigen presence were examined in various organs of control and antibody-treated neonatal AKR mice. The data graphically demonstrated that the treatment 'window' corresponded to a time just prior to the burst of ecotropic virus ICCs. The nature of ecotropic virus-positive cells and their elimination with treatment are discussed relative to later events in AKR leukemogenesis. (41 Refs)

10. INFLUENCE OF SELECTIVE ABSENCE OF H-2KKAPPA ON GROSS VIRUS LEUKAEMIAS IN VITRO AND THE IMPLICATIONS FOR IN VIVO SURVEILLANCE OF LEUKAEMIA.

Festenstein H, Schmidt W, Alonzo A, Leben L
Dept. Immunology, London Hosp. Medical Coll., London, England
Protides Biol Fluid Proc Colloq; 29:231-235 1982

Results are presented of direct complement dependent cytotoxicity tests using anti H-2Kkappa (H-2Kk) monoclonal antibody on five primary AKR leukemias. These and earlier results permit the conclusion that the absence/reduction of the H-Kk gene product is not uncommon in Gross virus leukemia. In search of the biological implication of this finding, a comparison was made of the ability of the K-GV BALB/c Gross virus tumor, which lacks Kk, and other Gross virus tumors with normal H-2Kk representation, to act as targets in cell mediated lympholysis (CML). Results showed that resistance to syngeneic CML is apparently due to the absence of Kk and is thus a failure of associative recognition. Results suggest a new mechanism of escape of T cell surveillance by leukemic cells which involves selective decrease of the H-2Kk antigens, which in this and other studies, have been shown to serve as elements of associative recognition in Gross virus leukemia. (6 Refs)

11. MONOCLONAL ANTIBODY AGAINST EBV-ASSOCIATED TRANSFORMATION ANTIGEN DETECTED IN VITRO AND IN VIVO.

Thorley-Lawson DA, Geilinger K, Schooley R
Div. Geographic Medicine, Tufts Univ. Sch. Medicine, Boston, MA, 02111
Protides Biol Fluid Proc Colloq; 29:739-742 1982

Transformation antigens on the surface of in vitro Epstein-Barr virus (EBV)-transformed B lymphocytes were defined by producing specific monoclonal antibodies. A hybridoma (17D6) was cloned and analyzed for its binding properties to a variety of EBV-positive and -negative B cell lines. The antibody reacted strongly with all of the EBV-positive lines and weakly with the EBV-negative lines. Similarly, a panel of EBV-negative cell lines from a variety of sources reacted only weakly with the 17D6 antibody. When a whole panel of EBV-infected cells from sources other than in vitro infection were tested, all the cell lines containing EBV were as positive as in vitro infected cells, including one cell line derived by spontaneous outgrowth from an EBV-positive individual and one from co-cultivation of normal lymphocytes from a seronegative individual with a nasopharyngeal carcinoma. Burkitt's lymphoma tumor cells reacted only weakly with the 17D6 antibody due to their relatively low levels of the antigen. 17D6-positive cells also were detected in the peripheral blood of infectious mononucleosis (IM) patients. 17D6-positive cells could be detected in the peripheral blood of a patient with chronic EBV infection at higher levels than in patients with acute IM. After recovery, no 17D6-positive cells could be detected. Radioimmunoprecipitation studies suggested that the 17D6 antibody recognizes a polypeptide of 40,000 mol wt. The results indicated that the 17D6 antibody recognizes an EBV-associated transformation antigen on the surface of in vitro and in vivo infected cells. (4 Refs)

12. ANTIBODY-DEPENDENT CELL-MEDIATED CYTOTOXICITY TO HERPES SIMPLEX VIRUS-TRANSFORMED CELLS IN THE COURSE OF CERVICAL CARCINOMA.

Christenson B
Dept. Epidemiology, Natl. Bacteriological Lab., S-105 21 Stockholm, Sweden
Am J Epidemiol; 115(4):556-568 1982

The antibody-dependent cell-mediated cytotoxicity assay was used to determine whether humoral antibodies from women with cervical carcinoma in the presence of normal mononuclear cells could induce cytotoxicity to hamster embryo fibroblasts, originally transformed by herpes simplex virus Type 2 (HSV-2) (333-8-9), to a cervical carcinoma cell line (ME-180) and to a lung carcinoma cell line (A-549). Control groups consisted of 81 age-matched healthy women and 77 patients suffering from malignancies other than cervical carcinoma. Significant cytotoxicity to HSV-2-transformed cells was observed in sera from 20 of 28 (71%) surviving patients with cervical cancer who were followed with serum samples collected 6-24 mo after initial treatment. Comparison of serum samples obtained before initial treatment from 20 patients surviving the observation period of 60 mo or longer and from 20 patients who died during the observation period showed that the survivors had significantly higher cytolytic activity prior to treatment. Long-term survivors also showed a drop in cytolytic activity in sera obtained 30 mo or later after treatment. Patients with long survival but whose cancer finally caused death, had stronger cytolytic activity than those with short survival (24 mo or less). Patients with cervical cancer had significantly higher cytolytic activity to HSV-2-transformed cells and to the cervical carcinoma cells (ME-180) than age-matched control women and patients with malignancies other than cervical carcinoma. (Author abstract) (33 Refs)

13. ANTIBODY PATTERN TO HUMAN CYTOMEGALOVIRUS IN PATIENTS WITH ADENOCARCINOMA OF THE COLON.

Avni A, Haikin H, Feuchtwanger MM, Sacks M, Naggan L, Sarov B, Sarov I
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Intervirology; 16(4):244-249 1981

The role of human cytomegalovirus (CMV) was examined according to serological patterns in 37 patients with adenocarcinoma of the colon (ACC). The sera were examined for the presence of IgG antibodies by the immunoperoxidase antibody to membrane antigen (IPAMA) method and by the complement-fixation (CF) test. Antibody determinations were also performed by the IPAMA method for three other members of the herpesvirus group: Epstein-Barr virus (EBV), herpes simplex virus (HSV) and varicella-zoster virus (VZV). Comparison groups included normal subjects, ACC patients treated with chemotherapy, and patients operated on for benign diseases. No significant difference was found in the geometric mean titers (GMTs) for CMV and the other herpesvirus in the sera of nontreated ACC patients when compared with the control groups. However, a significantly elevated antibody titer to CMV was found in chemotherapy-treated ACC patients by both the IPAMA and CF methods. In this group, elevated titers were found by the IPAMA method for EBV and HSV, but not for VZV. The significance of serological studies in elucidating the role of CMV in ACC patients is discussed. (Author abstract) (30 Refs)

ANTITUMOR ACTIVITY AND IMMUNOTHERAPY

14. TUMOR-ASSOCIATED NEURAL DIFFERENTIATION ANTIGENS DETECTED ON C1300 NEUROBLASTOMA CELLS BY HYBRIDOMA MONOCLONAL AUTOANTIBODIES.

Revoltella RP, Businaro R, Lauro G, Toesca A
Lab. Cell Biology, CNR, Via G. Romagnosi 18/A, 00196 Rome, Italy
Cell Immunol; 68(1):75-92 1982

Immune isoantisera and hybridoma monoclonal autoantibodies against syngeneic C1300 neuroblastoma (NB) cells were produced from BALB/c mice. Isoantisera were obtained (i) from mice immunized with membrane preparations from cloned NB cells and (ii) from mice bearing NB tumors. After repetitive absorptions on several different syngeneic or allogeneic tumor cell lines and syngeneic normal kidney, liver, spleen, bone marrow, and brain mouse tissue powders, these sera still retained antibodies reacting with tissue-differentiation antigens present on both NB cells and normal nerve sympathetic cells on cryostat whole body sections of neonatal mice. Monoclonal autoantibodies against NB cells were the products of the fusion between plasmacytoma cells and spleen cells from mice bearing syngeneic NB tumors. These anti-NB monoclonal antibodies revealed a restricted spectrum of distinct alloantigenic specificities against syngeneic bone marrow, fetal and adult brain cells, and nerve sympathetic cells present on neonatal rather than adult mice. A mixture of four monoclonal antibodies, recognizing, respectively, an epitope of the Ia complex and three distinctive neuronal-restricted antigens, proved to be a powerful and specific probe for histological immunodiagnosis of neuroblastoma, on cryostat sections of NB tumors, metastases, and tumor-draining lymph nodes. (Author abstract) (34 Refs)

15. HLA ANTIGEN EXPRESSION ON UROTHELIAL CELLS: DETECTION BY ANTIBODY-DEPENDENT CELL-MEDIATED CYTOTOXICITY.

O'Toole CM, Tiptaft RC, Stevens A
Div. Immunology, Addenbrooke's Hosp., Laboratories Block, Hills Road, Cambridge, CB2 2QQ, England
Int J Cancer; 29(4):391-395 1982

Antibody-dependent cell-mediated cytotoxicity (ADCC) was used to detect HLA-A, -B and -C antigens on in vitro-cultured urothelial cells of normal or malignant derivation. Alloantisera induced specific lysis of 51Cr-labeled targets by effector lymphoid cells from non-immune donors. HLA antisera were routinely titered to dilutions greater than or equal to 10(-3) on urothelial cells in primary or long-term culture. The HLA phenotype was compared for lymphoid cells and urothelial cells from eight individuals. HLA antigens detected by complement mediated lymphocytotoxicity were also detected on urothelial cells. No deletions or gains in HLA antigens were found on normal or malignant urothelial cultures as compared with donor lymphocyte HLA typing. The results show that the established urothelial cell lines J82, TCCSuP and SCaBER have retained their donor HLA phenotype. The established cell lines T24 and RT4 derived from transitional cell carcinomas and HCV-29 from urothelium were found to have distinctive HLA profiles although donor lymphocytes were not available for comparison. The serological crossreactions seen in complement mediated lymphocytotoxicity were clearly observed in ADCC. In particular, HLA-Cw5 was found to crossreact with HLA-Cw8. HLA-Cw5 was detected on 6/8 cultures of transitional cell carcinomas and this was confirmed by absorption analysis. (Author abstract) (19 Refs)

16. IDENTIFICATION OF TUMOR-ASSOCIATED ANTIGENS ON ULTRAVIOLET LIGHT-INDUCED TUMORS USING ANTITUMOR ANTIBODIES DEVELOPED IN ASCITES FLUID.

Fortner GW, Takemoto LJ, Shehi L, Hansen JS
Div. Biology, Kansas State Univ., Manhattan, KS, 66506
Cancer Res; 42(6):2371-2375 1982

A method is described which leads to the production of large amounts of ascites containing antitumor antibody in small numbers of mice. The antibody was then used to identify and characterize tumor-associated antigens on an ultraviolet light-induced murine skin fibrosarcoma. The antibody showed specific complement-dependent cytotoxicity to the homologous tumor and to an allogeneic tumor line which displayed a glycoprotein viral determinant with a mol wt of 70,000 on its surface. Absorption of the immune ascites with other tumor cell lines removed the cytotoxicity in relation to the presence of the glycoprotein. Isolation of the tumor cell surface components binding antibody revealed two components with mol wt of approx 70,000 and 60,000. The Mr 70,000 component was identified as viral gp70 by peptide mapping. (Author abstract) (27 Refs)

17. A 94,000-DALTON GLYCOPROTEIN EXPRESSED BY HUMAN MELANOMA AND CARCINOMA CELLS.

Imai K, Wilson BS, Bigotti A, Natali PG, Ferrone S

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JNCI; 68(5):761-769 1982

The IgG2a monoclonal antibody (MoAb) 376.96S, secreted by a hybridoma derived from a mouse immunized with cultured human melanoma cells COLO 38, reacts with a single 94,000-dalton glycoprotein that is peripherally associated with the plasma cell membrane of cultured melanoma cells. Indirect immunofluorescence analysis with cryostat thin sections of human tissues showed that this antigen is absent from a large variety of normal tissues but is readily detectable on melanomas, nevi, and several different carcinomas. The MoAb376.96S binds with cultured melanoma and carcinoma cell lines to a similar extent and can mediate both complement-dependent and cell-dependent lysis of these cells. The 94,000-dalton glycoprotein detected by MoAb376.96S is distinct in its tissue distribution, antigenicity, and molecular profile from several structures previously identified with monoclonal antibodies that have similar molecular weights. (Author abstract) (24 Refs)

18. IN VITRO MONOCYTE MATURATION IN SQUAMOUS-CELL CARCINOMA OF THE LUNG: INFLUENCE OF HUMORAL FACTORS.

Dent RG, Cole PJ

Papworth Hosp., Papworth, Cambridgeshire, England

Br J Cancer; 45(4):522-530 1982

A previously described defect of in vitro monocyte maturation in patients with squamous-cell carcinoma of the lung (SCC) has been investigated further. The maturation of patients' monocytes in pooled normal human serum was significantly better than in autologous serum. Conversely, the maturation of normal control monocytes was significantly depressed in patients' serum. The defect has been shown to be due to the presence of an inhibitory factor, rather than the lack of a necessary component in the patients' serum. Artificially aggregated gamma-globulin inhibited monocyte maturation in vitro, but the presence of immune complexes in the serum of many patients with SCC did not correlate well with the depression of in vitro maturation of monocytes from the same patient. Similarly, pregnancy-associated alpha2-glycoprotein, in increased amounts in the serum of patients with SCC, showed no correlation with monocyte maturation. The addition of soluble extracts of tumor, but not of surrounding normal lung tissue significantly inhibited monocyte maturation. The results suggest that the defective monocyte maturation in patients with SCC is at least in part due to serum inhibitory factors, which are likely to be a heterogeneous group. (Author abstract) (34 Refs)

19. CYTOTOXICITY OF TUMOUR-BEARER SERUM TO D23 HEPATOMA CELLS DERIVED FROM SOLID TUMOURS, ASCITES OR IN VITRO CULTURES.

Lando P, Gabriel J, Berzins K, Perlmann P
Dept. Immunology, Univ. Stockholm, Stockholm, Sweden
Scand J Immunol; 15(3):259-266 1982

The complement-dependent cytotoxicity of antibodies in tumor-bearer serum (TBS) from rats carrying the chemically induced D23 hepatoma was investigated. Target cells were D23 cells from solid tumors (D23sol), from ascites tumors (D23asc), or from in vitro growing cell cultures (D23cc). The D23asc and D23cc cells were not lysed when used as target cells in the assay, although they evoke cytotoxic antibodies when growing in vivo. The D23 ascites cells became susceptible to complement-dependent lysis after trypsin treatment. This was, however, not due to unmasking of target antigens, since untreated D23 ascites cells absorbed cytotoxic antibodies as efficiently as trypsinized cells. No increase in susceptibility to complement-dependent lysis was observed after trypsin treatment of D23cc cells. Absorption of cytotoxic antibodies with D23cc cells showed no or very low antigen expression on the surface of these cells. They did, however, contain the antigen(s), since 3 M KCl extracts of the D23cc cells could inhibit the complement-dependent cytotoxicity of D23sol TBS against D23sol cells. From these data it was concluded that the susceptibility of hepatoma cells for antibody-mediated complement lysis is not only correlated with antigen expression, as was the case with the in-vitro-cultivated cells, but is also dependent on increased lytic susceptibility after trypsin treatment of the cells. (Author abstract) (26 Refs)

20. DIFFERENCES IN ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY AGAINST TUMOR CELLS IN IN VITRO DIFFERENTIATING MONONUCLEAR PHAGOCYTES FROM BONE MARROWS OF NORMAL AND INFLAMED MICE.

Bursuker I, Goldman R, Schade U, Lohmann-Matthes ML
Dept. Membrane Res., Weizmann Inst. Science, Rehovot, Israel
Cell Immunol; 68(1):53-63 1982

Mononuclear phagocytes, differentiated in vitro from bone marrow cells of mice inflamed in vivo with either Corynebacterium parvum or thioglycollate, expressed a higher activity in antibody-dependent cellular cytotoxicity (ADCC) against tumor cells, than those of normal mice. A good correlation between the cytolytic activity and chemiluminescence activity of the different mononuclear phagocyte populations was observed. The ADCC activity of BMDMP from normal mice was inhibited by exogenous prostaglandin E2 (PGE2) to a higher extent than that of BMDMP of inflamed mice. When the three BMDMP populations were cultured in the presence of aspirin (without exogenously added PGE2), the ADCC was significantly increased. The three populations gave identical high values. This suggests that the differential ADCC activity of BMDMP from normal and inflamed mice is due to their differential response to endogenous prostaglandins. PGE2 showed also a differential effect on the mononuclear phagocyte-forming capacity of bone marrow macrophage precursor cells from normal and inflamed mice. Bone marrow precursor cells from inflamed mice showed a higher resistance to the suppressive effect of PGE2 (10(-5) M) on mononuclear phagocyte-forming capacity than those of normal mice which were totally suppressed. It is concluded that the observed differential properties of the three bone marrow-derived mononuclear phagocyte populations originate at the level of bone marrow precursor cells and that, therefore, the similar functional differences observed in inflammation-induced peritoneal macrophage populations, observed by our and other groups, stem at least partly from differences at the level of bone marrow precursor cells. (Author abstract) (31 Refs)

21. CHARACTERIZATION AND USE OF AN ALLOTYPE-SPECIFIC MONOCLONAL ANTIBODY TO PLACENTAL ALKALINE PHOSPHATASE IN THE STUDY OF CANCER-RELATED PHOSPHATASE POLYMORPHISM.

Millan JL, Stigbrand T, Ruoslahti E, Fishman WH
Dept. Physiological Chemistry, Univ. Umea, S-901 87 Umea, Sweden
Cancer Res; 42(6):2444-2449 1982

The hybridoma technique was used to produce an allotype-specific monoclonal antibody (F11) that reacts with the products of the S, I, and D alleles of PLAP but not of the F allele. Serum and ascites samples from patients with different cancers containing high levels of PLAP were tested for reactivity with F11. These tumor-derived PLAPs were of the Nagao type as shown by their sensitivity to inhibition by L-leucine. This type of inhibition is exhibited also by the rare D allelic variant of PLAP but not by the common forms. Thus, it has been proposed that the Nagao enzyme represents reexpression of the D allele of PLAP. F11 reactive and nonreactive samples as well as samples with intermediate reactivity were found among the cancer sera and ascites. Our results show that the tumor-derived Nagao enzyme does not represent the reexpression of the D allele but instead, in spite of its distinct inhibition pattern, expresses the same genetic polymorphism that is found in the placenta. (Author abstract) (28 Refs)

22. INFLUENCE OF THE LIVER ON THE PROFILE OF CIRCULATING ANTIGENS RECOGNIZED BY ANTISERUM AGAINST HEPATOMA MEMBRANE GLYCOPROTEINS.

Baumann H, Eldredge D
Dept. Cell and Tumor Biology, Roswell Park Memorial Inst., Buffalo, NY, 14263
Cancer Res; 42(6):2398-2406 1982

Rat hepatoma tissue culture cells have retained only a few liver-specific membrane functions. To find out whether transformation of these cells led to the appearance of tumor-specific membrane glycoprotein structures, which might also be present in released form in the circulation of tumor-bearing animals, we compared immunologically the sera and ascites fluids of normal and of hepatoma-bearing rats. For structural identification, we used polyspecific antibodies against the membrane glycoproteins of the hepatoma cells. Crossed immunoelectrophoresis of the body fluids resulted in the separation of several antigens, one of which appears to be tumor specific. Immunoelectrophorectic analyses of the glycoproteins from the membranes of liver and hepatoma cells revealed many shared antigens; in one instance, we could assign the membrane associated form to major antigen detected in the serum. Characterization of the molecular size and charge of two selected antigens by two-dimensional gel electrophoresis indicated that the hepatoma cell products were not completely sialylated. In the case of the circulating, hepatoma-specific antigen, this property appears to result in hepatic clearance of the most basic ('asialo') portion of the glycoprotein species via the receptor-mediated uptake of galactose-terminated glycoproteins. The result was the accumulation of the acidic forms of the antigen in the serum and ascites fluid of tumor-bearing rats. (Author abstract) (19 Refs)

23. INFILTRATION OF LYMPHOSARCOMA CELLS INTO HEPATOCYTE CULTURES: INHIBITION BY UNIVALENT ANTIBODIES AGAINST LIVER PLASMA MEMBRANES AND LYMPHOSARCOMA CELLS.

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Div. Cell Biology, Netherlands Cancer Inst., Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands
Protides Biol Fluid Proc Colloq; 29:313-316 1982

Identification of cell surface components involved in the infiltration of mouse MB 6A lymphosarcoma cells (MBLC) was studied in cultures of isolated rat hepatocytes. Antisera were raised in rabbits against contiguous face-enriched rat liver plasma membranes (LPM), against whole lymphosarcoma cells, and against sinusoidal face-enriched LPM. Infiltration of the MBLC into cultures of the isolated hepatocytes was inhibited by univalent antibodies (Fab fragments from rabbits) directed against rat liver plasma membranes (anti-LPM) and against MBLC (anti-MBLC). Anti-MBLC and an anti-LPM, raised against sinsusoidal face-enriched LPM, reduced the number of infiltrating MBLC solely by inhibiting adhesion of MBLC to the exposed hepatocyte surface. However, anti-LPM raised against contiguous face-enriched LPM not only reduced adhesion to the exposed surface, but also the subsequent infiltration of the adherent cells. MB 6A cells may adhere to two different hepatocyte components, one of which may be present only at the contiguous surface. A high affinity of the latter component could explain the diffuse growth pattern of MBLC in the intact liver. (10 Refs)

24. MONOCLONAL ANTIBODIES TO TUMOR-ASSOCIATED GLYCOLIPIDS: PREPARATION AND APPLICATION FOR SUPPRESSION OF TUMOR GROWTH.

Young WW, Urdal DL, Hakomori S
Biochemical Oncology, Fred Hutchinson Cancer Res. Center, Seattle, WA, 98104
Protides Biol Fluid Proc Colloq; 29:809-811 1982

A ceramide trisaccharide, gangliotriosylceramide (GOC) was found to be specific for mouse lymphoma L5178Y and mouse sarcoma KiMSV. Two monoclonal antibodies and polyclonal antibodies directed to this glycolipid were used for suppression of tumor growth in vivo and targeting of drugs to tumor in vitro. Growth of mouse lymphoma L5178Y (which contains large quantities of GOC) in DBA/2 mice was suppressed by passive immunization with monoclonal immunoglobulin G3 antibodies to GOC, but not by IgM antibodies, with or without added complement. (11 Refs)

25. MOLECULAR HETEROGENEITY OF A HIGH MOLECULAR WEIGHT HUMAN MELANOMA ASSOCIATED ANTIGEN DETECTED BY MONOCLONAL ANTIBODIES.

Imai K, Wilson BS, Ruberto G, Nakanishi T, Yachi A, Ferrone S
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Protides Biol Fluid Proc Colloq; 29:893-897 1982

The spatial relationship among antigenic determinants recognized by four monoclonal antibodies (MoAbs) specific for a human high mol wt melanoma-associated antigen (MAA) was analyzed. The four MoAbs were compared in direct and indirect inhibition binding assays to determine whether they identified the same or different antigenic determinants. MoAbs 138.13S, 225.28S, and 653.40S recognized the same or closely associated antigenic determinants which were distinct from that recognized by MoAb 763.24T. Sequential immunodepletion studies demonstrated that the high mol wt MAA may be divided into three subpopulations: Group 1 carries the antigenic determinants recognized by the MoAb 138.13S (225.28S or 653.40S) and 763.24T; Group 2 carries only the determinants recognized by MoAb 138.13S (225.28S or 653.40S); and Group 3 carries only the determinants recognized by the MoAb 763.24T. The amount of high mol wt molecules in each subpopulation was in the order of Group 1 greater than Group 2 greater than Group 3. (7 Refs)

26. REACTIONS OF MONOCLONAL ANTIBODIES AGAINST HUMAN MELANOMA WITH DIFFERENT TISSUES AND CELL LINES.

Hageman P, Vennegoor C, Van der Valk M, Landegent J, Jonker A, Van der Mispel L
Div. Clinical Oncology, The Netherlands Cancer Inst., Amsterdam, The Netherlands
Protides Biol Fluid Proc Colloq; 29:889-892 1982

Spleen cells from a BALB/c mouse immunized with plasma membrane from the human melanoma cell line MeWo were fused with the IgG-1 producing mouse myeloma cell line P3X63Ag8. Antibodies from seven hybridomas were tested for their reactions on various cell lines and tissues. The antibodies reacted with many melanoma cell lines but did not show high specificity in the 125I-F(ab')2 anti-mouse IgG binding assay; they reacted with a number of control tumor and normal cell lines. Sera were tested with an immunoperoxidase sandwich test on thin sections of frozen tissue from melanoma metastases; mammary tumors; normal skin, brain, lung and mammary gland; fetal tissues; and mammary tissues of dog, cat and mouse. Four distribution patterns were observed: one hybridoma produced antibodies with a broad tissue distribution and the reaction was directed against an 88,000 dalton protein; two groups of antibodies reacted primarily with metastatic melanomas; and one antibody reacted with melanoma and other tissues, particularly human mammary tumor. (8 Refs)

27. SPECIFIC KILLING OF HUMAN AND MOUSE TUMOR CELLS BY IMMUNOTOXINS.

Casellas P, Blythman HE, Brown JP, Gros O, Gros P, Hellstrom KE, Hellstrom I, Jansen FK, Poncelet P, Vidal H
Centre de Recherches CLIN MIDY, Monpellier, France
Protides Biol Fluid Proc Colloq; 29:927-932 1982

Monoclonal antibodies (anti-Thy 1.2 and anti-human melanoma P97) were used to replace the binding moiety of the B-chain of ricin, in order to obtain immunotoxins that use the purified A-chain of ricin as the toxic moiety. The A-chain was coupled to the antibodies via a disulfide linkage, allowing a linkage of active A-chain to antibody ratio of 3:1 for IgM anti-Thy 1.2 and 1.4:1 for the IgG anti-melanoma immunotoxin. Both immunotoxins showed specific cytotoxicity for their respective target cells. In vitro tests of protein synthesis inhibition and of inhibition of colony formation demonstrated the specific activity of the immunotoxins. Both immunotoxins could specifically kill the last target cell without damaging control cells, and a specific killing index could be calculated. The loss of binding capacity due to conjugation was estimated to be 10% for anti-Thy 1.2 immunotoxin and 30% for anti-melanoma immunotoxin. (11 Refs)

28. THE POTENTIAL USE OF MONOCLONAL ANTIBODIES IN DRUG TARGETING.

Rowland GF, Simmonds RG, Corvalan JR, Marsden CH, Johnson JR, Woodhouse CS, Ford CH, Newman CE

Lilly Res. Centre, Erl Wood Manor, Windlesham, Surrey, England

Protides Biol Fluid Proc Colloq; 29:921-926 1982

Conjugates of vindesine (VDS) and polyclonal antibodies were prepared. In vitro targeting was demonstrated with an indirect or 'sandwich' technique. VDS-goat anti-rabbit conjugates were used with either mouse T lymphoma cells (EL4) or human anaplastic lung tumor cells (CALU-6). Cells were exposed to appropriate rabbit antiserum for 30 min, unbound antibody was washed away, and the cells were further incubated with VDS-goat anti-rabbit antibody. The number of EL4 cells increased during the first 24 hr of growth following such treatment. Similar results were obtained with CALU-6 cells following 2 hr of incubation. Cytostatic effects were obtained in both cell types only when the VDS conjugate could recognize the first layer antibody as a target. When VDS-sheep anti-carcinoembryonic antigen (CEA) IgG was used, the VDS-antibody conjugate was more cytotoxic than free VDS, mixtures of VDS and antibody, or a conjugate of VDS and normal sheep IgG. Approx 25x less conjugated VDS was necessary than free VDS to kill 50% of the cells. Several fusions were attempted in order to produce specific monoclonal anti-CEA antibodies; a high yield of active hybridomas was achieved. (10 Refs)

29. ENRICHMENT OF HUMAN MARROW LYMPHOCYTES WITH MONOCLONAL ANTIBODIES TO MURINE ANTIGENS.

Landreth KS, Kincade PW, Lee G, Gathings WE, Fu SM

Sloan-Kettering Inst. Cancer Res., 145 Boston Post Road, Rye, NY, 10580

Proc Natl Acad Sci USA; 79(7):2370-2374 1982

Two monoclonal antibodies, prepared against a murine B lymphoma and characterized as binding to a cell surface antigen represented primarily on cells of the B lineage, were found to bind to human hemopoietic cells. These antibodies recognize similar populations of cells in mice and humans. Antibodies from clones 177.17 and 83.4 bound to 6% of human bone marrow nucleated cells. This included all cells with detectable cell surface Ig (sIg+) and those that lack sIg but have detectable cytoplasmic mu (sIg-, cmu+), considered to be the immediate precursors of B lymphocytes (pre-B cells). In addition, these antibodies bound to a subpopulation of T cells and a proportion of null lymphocytes in marrow, spleen, and peripheral blood. An unexpected finding was that established pre-B cell lines were not recognized by these antibodies and possible reasons for this are considered. By using antibody-coated polystyrene plates for cell depletion and recovery, highly enriched preparations of cmu+, sIg- cells have been obtained. These antibodies and enrichment procedures should prove valuable in establishing the minimal requirements for maturation of these putative precursors in vitro, for comparative studies of immunodeficiency/autoimmune diseases in man and experimental animal models, and for monitoring the outcome of therapeutic marrow transplantation. (Author abstract) (24 Refs)

30. TUMOUR LOCALIZATION OF MONOCLONAL ANTIBODY AGAINST A RAT MAMMARY CARCINOMA AND SUPPRESSION OF TUMOUR GROWTH WITH ADRIAMYCIN-ANTIBODY CONJUGATES.

Pimm MV, Jones JA, Price MR, Middle JG, Embleton MJ, Baldwin RW

Cancer Res. Campaign Laboratories, Univ. Nottingham, Nottingham, NG7 2RD, England

Cancer Immunol Immunother; 12(2):125-134 1982

The tumor-localizing potential of Sp4/A4 monoclonal antibody to the rat mammary carcinoma Sp4 isolated from hybridoma supernatants was established and the therapeutic effectiveness of the monoclonal antibody conjugated to the broad-spectrum anti-tumor agent adriamycin (ADR) was assessed. Characterization of SP4/A4 is described. Following iv injection of 125I-Sp4/A4 antibody into normal WAB/Not rats, blood levels of the antibody dropped to 50% over the first 5 hr and then decreased more slowly, with a half-life of 40 hr. Urinary excretion averaged 18% of injected dose over the first 24 hr and showed similar rates over the next 3 days. Raised levels of Sp4/A4 were found in tumor tissue of rats with sc growths of SP4 as compared with lung, liver, spleen, kidney, and heart. The time course of 125I-Sp4/A4 uptake was examined. When rats bearing other tumors were included, levels of radioactivity in Sp4 tumor growths exceeded those in any of the organs examined, and the activity in other tumors was comparable to that in visceral organs. No preferential localization of 125-I-labelled normal rat immunoglobulin was observed in Sp4 tumors. Treatment of Sp4 tumor cells with Sp4-A4 antibody did not inhibit their growth in syngeneic rats; treatment of hosts with antibody similarly had no inhibitory effect on growth of an sc tumor challenge. Treatment of Sp4 cells with ADR-monoclonal antibody conjugates significantly retarded Sp4 tumor growth. The results indicated that monoclonal antibody directed against tumor cell surface antigens may be highly effective for tumor targeting of therapeutic agents. (22 Refs)

31. GD3, A PROMINENT GANGLIOSIDE OF HUMAN MELANOMA. DETECTION AND CHARACTERIZATION BY MOUSE MONOCLONAL ANTIBODY.

Pukel CS, Lloyd KO, Travassos LR, Dippold WG, Oettgen HF, Old LJ

Memorial Sloan-Kettering Cancer Center, New York, NY, 10021

J Exp Med; 155(4):1133-1147 1982

Mouse monoclonal antibody AbR24 has a high degree of specificity for human melanoma cells when tested on viable cell cultures. The protein A mixed hemagglutinin serological assay demonstrated an antigen detected AbR24, shown to be GD3 ganglioside by compositional and partial structural analysis and by comparison with authentic GD3 in thin layer chromatography. AbR24 reacted with authentic GD3 but not with any of the other standard gangliosides tested. Melanomas have a characteristic pattern of gangliosides; in all lines examined, glycolipids comigrating with GD3 and GM3 were prominent acidic glycolipids, with GD3 being the major component in many of the lines. GD3 was also prominent in extracts of mouse eye and bovine choroid. The only other line that had GD3 as the major component was MOLT-4 (a T cell line). Compared with 7% in the adult human brain, 9% in a renal cancer cell line, 11% in RAJI cells, and 33% in MOLT-4 cells, GD3 constituted 18-63% of the total ganglioside fraction in the melanoma cell lines. The 125I-protein A mixed hemagglutinin serological assay detected GD3 in all the cells and tissues examined. The apparent discrepancy between the ubiquitous presence of GD3 and the serological specificity of AbR24 for melanoma cells was explained by the localization and concentrations of GD3 in different cells. (31 Refs)

32. TISSUE DISTRIBUTION AND MOLECULAR PROFILE OF A DIFFERENTIATION ANTIGEN DETECTED BY A MONOCLONAL ANTIBODY (345.134S) PRODUCED AGAINST HUMAN MELANOMA CELLS.

Imai K, Natali PG, Kay NE, Wilson BS, Ferrone S
(c/o Ferrone) Dept. Pathology, Coll. Physicians and Surgeons, Columbia Univ., 630 West 168th St., New York, NY, 10032
Cancer Immunol Immunother; 12(2):159-166 1982

The mouse IgG2a monoclonal antibody (MoAb) 345.134S secreted by a hybridoma derived from a mouse immunized with cultured human melanoma cells was examined in relation to the structure of the target antigen. The distribution of the antigen in normal and malignant tissues, and the expression of the antigen on cultured cells and its ability to function as a target of immune lysis was also studied. The structure detected by the MoAb 345.134S is composed of an 85 kilodalton (KD) glycopolypeptide linked by disulfide bridges with a 30 KD polypeptide carrying little or no carbohydrate. The 115 KD antigen appears to be peripheral rather than integral to the plasma membrane. Indirect immunofluorescence studies showed that the reactivity pattern of normal tissues with MoAb 345.134S does not correlate with their embryological origin. The majority of normal tissues gave only weak staining with MoAb 345.134S. All the types of tumors tested, except liver adenocarcinomas, reacted strongly with MoAb 345.134S, although there were some cases within each tumor group that were negative. MoAb 345.134S reacted in a radioimmunometric assay with a variety of cell lines, including melanoma, carcinoma, and lymphoid types. There was no relationship between the level of expression of the antigenic determinant recognized by MoAb 345.134S and other surface markers tested. The level of antigen detected by MoAb 345.134S was unchanged in the presence of interferon but was decreased by puromycin exposure. The opposite was true for cell-dependent lysis of cultured human cells. (32 Refs)

IMMUNOGLOBULIN STRUCTURE AND SYNTHESIS

33. RECEPTORS FOR IGA ON RABBIT LYMPHOCYTES. II. CHARACTERIZATION OF THEIR BINDING PARAMETERS FOR IGA.

Stafford HA, Knight KL, Fanger MW
Dept. Microbiology and Medicine, Dartmouth Medical Sch., Hanover, NH, 03755
J Immunol; 128(5):2201-2205 1982

The specificity of rabbit receptors for IgA (RFcalpha) was investigated on lymphocytes isolated from the Peyer's patches and spleen. Specificity was determined by the inhibition of IgA rosette formation with intact and proteolytic fragments of rabbit and human secretory IgA (SIgA), human myeloma proteins, and secretory component. RFcalpha bound human SIgA as efficiently as rabbit SIgA. Of the human IgA tested, RFcalpha preferentially bound to the IgA2 subclass and mostly avidly to a multimeric IgA molecule. In addition, the site of RFcalpha-IgA interaction was localized to the Calpha2 domain in the Fc portion of IgA. RFcalpha on spleen lymphocytes showed the same pattern of binding specificity toward the human IgA subclasses as the RFcalpha on lymphocytes from Peyer's patches. However, differences between the spleen and Peyer's patches were observed in the interaction of RFcalpha and the rabbit IgA subclasses. RFcalpha on lymphocytes from the Peyer's patches bound the rabbit IgA-g subclass more efficiently than the rabbit IgA-f subclass, whereas the converse was true for the spleen RFcalpha. Human secretory component inhibited IgA but not IgG or IgM rosette formation as a result of its interaction with lymphocytes. These studies suggest: (1) that there may be two types of RFcalpha expressed by lymphocytes in certain tissues, and (2) that there are two closely associated receptors on the lymphocyte - one specific for secretory component and the other for structures within the Calpha2 domain of IgA. (Author abstract) (20 Refs)

34. FC RECEPTORS FOR IGE ON MOUSE MACROPHAGES AND MACROPHAGE-LIKE CELL LINES.

Boltz-Nitulescu G, Plummer JM, Spiegelberg HL
Inst. General Experimental Pathology, Univ. Vienna, Wahringerstrasse 13, A 1090 Vienna, Austria
J Immunol; 128(5):2265-2268 1982

Murine alveolar and peritoneal macrophages (AMphi, PMphi) and Mphi-like cultured cell lines were analyzed for IgE Fc receptors by rosette formation with mouse IgE-sensitized red cells and by binding of radiolabeled mouse IgE. A mean of 90.4% AMphi, 56.9% PMphi, 93.4% P388D1, 81.2% J744.1, 15.6% WEH13, 54.7% WR19M.1, 52.3% RAW264.7, and 19.5% RAW309Cr.1 Mphi-like cells formed IgE rosettes. The rosettes were specific for native mouse IgE and were inhibited by mouse IgE but not mouse IgG, IgA, IgM, or heat-denatured mouse IgE. Rat IgE, but not human IgE, induced rosettes and inhibited mouse IgE rosettes. Trypsin treatment of the Mphi abolished IgE rosette formation. Mouse IgE bound to P388D1 Mphi-like cells with a KA of 7.6 +-0.2 x 10(6) M-1 to 3.3 +-0.9 x 10(5) binding sites. After 30 min of incubation at 37 C, 30 to 45% of AMphi, P388D1, and J774.1 Mphi-like cells ingested erythrocytes sensitized with IgE but not unsensitized erythrocytes. The data indicate that mouse Mphi bear Fc receptors specific for IgE that mediate phagocytosis of IgE-sensitized erythrocytes. (Author abstract) (29 Refs)

35. MODULATION OF CHRONIC LYMPHOCYTIC LEUKEMIA CELLS BY PHORBOL ESTER: INCREASE IN IA EXPRESSION, IGM SECRETION AND MLR STIMULATORY CAPACITY.

Okamura J, Letarte M, Stein LD, Sigal NH, Gelfand EW
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J Immunol; 128(5):2276-2280 1982

When cultured with 12-O-tetradecanoylphorbol 13-acetate (TPA) at a concentration of 1.6 x 10(-7) M, chronic lymphocytic leukemia (CLL) cells differentiated into mature cells of B lineage and increased their expression of surface Ia antigens when compared with cells cultured in the absence of TPA. Concurrently, TPA enhanced the ability of CLL cells to stimulate in a mixed lymphocyte reaction (MLR). The events induced in vitro by TPA that are characteristic of B cell maturation included morphologic changes, reduction in surface immunoglobulin (Ig), appearance of cytoplasmic Ig, and secretion of IgM. The increase in Ia expression and the enhanced capacity to stimulate in an MLR after incubation with TPA might also be associated with maturation of the CLL cells. The changes induced in vitro by TPA in neoplastic B cells provide new information concerning the terminal events in normal B cell differentiation. (Author abstract) (24 Refs)

36. HYALINE INCLUSIONS (PSEUDOPSAMMOMA BODIES) IN MENINGIOMAS: IMMUNOCYTOCHEMICAL DEMONSTRATION OF EPITHELIAL-LIKE SECRETION OF SECRETORY COMPONENT AND IMMUNOGLOBULINS A AND M.

Budka H
Inst. Neurology, Univ. Vienna, Schwarzspanierstr. 17, A-1090 Vienna, Austria
Acta Neuropathol (Berl); 56(4):294-298 1982

Three of eight meningotheliomatous meningiomas studied by routine histology and immunocytochemistry (indirect immunofluorescence, peroxidase antiperoxidase method) contained pseudopsammoma bodies (PPB). PPB were eosinophilic, nondigestible PAS-positive globules of variable size and density. Intracellularly, single bodies and multiple, mulberry-shaped aggregates were seen. PPB showed strong reactions with antisera to human secretory component (SC), IgA, and IgM. Most PPB stained for SC, less for IgA, and less for IgM. Labeling was mainly homogeneous. Inclusions were often surrounded by a thin membrane-like structure. In one case, PPB were positive for albumin but,not for IgG. The labeling observed was similar to that of intracytoplasmic globules of a metastatic carcinoma and gastric and mammary carcinoma cells. In carcinoma cells, development of intracellular globules is due to epithelial cells retaining their ability of SC production and uptake and secretion of immunoglobulins. These findings support the concept of secretory differentiation in meningiomas, and demonstrates an epithelial character in at least some meningiomas. (14 Refs)

37. PROTEIN A REACTIVITY OF LYMPHOCYTES FROM SOME PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKAEMIA MEDIATED BY AN INTERACTION WITH THE F(AB')2 REGION OF SURFACE IMMUNOGLOBULIN.

Romagnani S, Giudizi MG, Biagiotti R, Almerigogna F, Del Prete GF, Maggi E, Ricci M
(c/o Ricci) Immunologia Clinica, Istituto Clinica Medica 3, Policlinico Careggi, 50134-Firenze, Italy
Scand J Immunol; 15(3):287-295 1982

Peripheral blood lymphocytes (PBL) from 15 of 38 patients with chronic lymphocytic leukemia (CLL) were capable of forming rosettes with human erythrocytes coated with staphylococcal protein A (SpA-HRBC). PBL from seven patients also showed a marked proliferative response after stimulation with Staphylococcus aureus bacteria strain Cowan I (Cowan Staph). The SpA-rosetting of CLL cells was inhibited by incubation with F(ab')2 fragments of anti-immunoglobulin (Ig) antibodies. In addition, incubation with these fragments inhibited the proliferative response of leukemic B cells to Cowan Staph. The Cowan-Staph-induced proliferation of CLL cells was also impaired by the addition of normal human IgG and human IgG F(ab')2 fragments to the cultures, whereas non-immune rabbit IgG was not inhibitory. The inhibitory activity of human IgG F(ab')2 fragments was retained by a SpA-Sepharose column, and it was found in the material recovered from the same column by acid elution. These data indicate that an interaction between SpA and a structure located in the F(ab')2 region of surface Ig of different classes is responsible for either SpA-binding or the Cowan-Staph-induced proliferative response of PBL from some patients with CLL. (Author abstract) (24 Refs)

38. ASSOCIATION CONSTANTS OF HYBRIDOMA ANTIBODIES SPECIFIC FOR ALPHA(1 TO 6) LINKED DEXTRAN DETERMINED BY AFFINITY ELECTROPHORESIS.

Sharon J, Kabat EA, Morrison SL
Dept. Microbiology, Inst. Cancer Res., Columbia Univ., Coll. Physicians and Surgeons, New York, NY, 10032
Mol Immunol; 19(3):389-397 1982

Binding constants of monomers of seven BALB/c IgM, four BALB/c IgA, and one C57BL/6 IgA anti-alpha (1 to 6) dextran hybridoma antibodies with dextran B512 and with isomaltoheptaose were determined by affinity electrophoresis. Binding constants to dextran range from 1.52 x 10(5) to 4.43 x 10(5) ml/g for the five IgA monomers and from 1.70 x 10(3) to 6.10 x 10(4) ml/g for the seven IgM monomers. Antibody monomers containing both specific and nonspecific (drived from the myeloma cell that was used to generate the hybridomas) light chains are shown to have association constants with dextran 6 to 30-fold lower than monomers containing only specific light chain, suggesting that the association of specific heavy chain with nonspecific light chain does not result in an antidextran combining site. Binding constants with isomaltoheptaose range from 1.45 x 10(4) to 7.01 x 10(4)/M for the IgA proteins and from 6.46 x 10(3) to 7.70 x 10(4)/M for the IgM proteins. The binding constants with dextran and with isomaltoheptaose, and the electrophoretic, immunochemical and idiotypic characteristics of the hybridoma proteins are discussed. (Author abstract) (23 Refs)

39. IMMUNOCHEMICAL CHARACTERIZATION OF BINDING SITES OF HYBRIDOMA ANTIBODIES SPECIFIC FOR ALPHA(1 TO 6) LINKED DEXTRAN.

Sharon J, Kabat EA, Morrison SL
Dept. Microbiology, Inst. Cancer Res., Columbia Univ. Coll. Physicians and Surgeons, New York, NY, 10032
Mol Immunol; 19(3):375-388 1982

The combining sites of seven BALB/c IgM, four BALB/c IgA and one C57BL/6 IgA hybridoma antibodies specific for alpha(1 to 6) linked dextran were probed by precipitin and precipitin inhibition assays. The 12 antibodies are able to bind to linear determinants in the interior of the dextran molecule; some have sites complementary to six alpha(1 to 6) linked glucose residues and others have sites complementary to seven alpha(1 to 6) linked glucose residues. From the analysis of the precipitins and precipitin inhibitions, it is concluded that no two hybridoma proteins have identical binding sites. (Author abstract) (45 Refs)

40. EXPRESSION AND DYNAMICS OF MEMBRANE IMMUNOGLOBULINS.

Pernis B, Roth P
Dept. Microbiology, Coll. Physicians and Surgeons, Columbia Univ., New York, NY
Pharmacol Rev; 34(1):65-72 1982

Membrane immunoglobulins on B lymphocytes, membrane IgD, simultaneous expression of messenger IgM and IgD, and internalization or shedding of cross-linked membrane IgM and IgD in human B lymphoid cells are discussed. Important information on the effects of interactions with messenger Ig on B cell differentiation has been derived from experiments in which anti-immunoglobulin antibodies could block specific antibody production in an in vitro immune response as well as differentiation to immunoglobulin-secreting cells in mitogen-activated lymphocyte cultures. (162 Refs)

41. IMMUNOGLOBULIN ALLOTYPES IN PATIENTS WITH SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK.

Ockhuizen T, Pandey JP, Veltri RW, Arlen M, Fudenberg HH
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Cancer; 49(10):2021-2024 1982

Gm, A2m, and Km allotypic markers were examined in 40 Caucasian patients with squamous cell carcinoma of the head and neck. Serum IgA levels, the A2m(1) allotypic marker, and antibodies against IgA1, A2m(1), and A2m(2) were measured quantitatively. The frequency of Km(1) was found to be significantly increased in patients with head and neck cancer as compared to the control population. (Author abstract) (38 Refs)

42. DISTRIBUTION OF IMMUNOGLOBULIN-CONTAINING CELLS AND LOCALIZATION OF SECRETORY COMPONENT IN GASTRIC MUCOSA BEARING CARCINOMA.

Togo S, Hirayama R, Hirokawa K
Second Dept. Surgery, Faculty Medicine Tokyo Medical and Dental Univ., Tokyo, Japan
Bull Tokyo Med Dent Univ; 28(2):61-75 1981

Surgical material from 80 patients with gastric carcinoma (GC) was examined by the direct immunofluorescent antibody technique and indirect peroxidase-labeled antibody technique to determine the distribution of immunoglobulin-containing cells and localization of the secretory component (SC). Distribution of immunoglobulin-containing cells was studied in the lamina propria surrounding GC and the stroma of GC tissue. Types of carcinoma examined included well, moderately and poorly differentiated carcinoma and signet-ring cell carcinoma. There was no convincing evidence which suggested that the secretory immune system surrounding carcinoma was responding to the tumor. In some cases increase of IgG-containing cells in the stroma of carcinoma suggested some kind of tumor immunity. In the non-carcinomatous mucosa, SC was observed strongly in cells of intestinal metaplasia (except for goblet cells), but only weakly in normal foveolar epithelium. SC was observed in 45% (36/80) of the total cases of GC, and was especially prominent in signet-ring cell carcinoma (78%). IgA was found in about 50% of these SC-positive carcinomas. SC was also frequently positive in Group III atypical epithelium. (22 Refs)

43. DISTRIBUTION OF IGM, IGA AND IGG SECRETING CELLS IN THE TISSUES OF NORMAL AND TUMOR-BEARING MICE.

Howie S, McBride WH, James K
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Immunology; 46(1):43-48 1982

The levels of IgM, IgA and IgG secreting cells were examined in control, Corynebacterium parvum-stimulated and tumor-bearing, normal and athymic (Nu/Nu) mice. The percentage of IgA to IgM or IgG secreting cells is relatively higher in peripheral blood than in the spleen or peritoneum of normal mice. Within tumors, irrespective of their degree of vascularization and immunogenicity, the pattern of Ig secreting cells is similar to that seen in peripheral blood and different from that in spleen and peritoneum even in athymic mice. Intraperitoneal injection of C parvum changes the relative percentages of Ig secreting cells in the peritoneal cavity to resemble that seen in the peripheral blood and tumors. It appears that Ig secreting cells extravasate from peripheral blood in a non-isotype specific manner into sites of chronic stimulation. (Author abstract) (11 Refs)

44. IMMUNOHISTOCHEMICAL EVALUATION OF CARCINOEMBRYONIC ANTIGEN, SECRETORY COMPONENT, AND EPITHELIAL IGA IN ULCERATIVE COLITIS WITH DYSPLASIA.

Rognum TO, Elgjo K, Fausa O, Brandtzaeg P
Histochemical Lab., Inst. Pathology, Rikshospitalet, Oslo 1, Norway
Gut; 23(2):123-133 1982

Immunofluorescence staining for carcinoembryonic antigen, secretory component, and epithelial IgA was evaluated semiquantitatively in routine formalin-fixed mucosal biopsy samples from five patients with ulcerative colitis who had undergone colectomy because of carcinomas. The two types of lesion did not differ significantly with regard to the expression of the three marker antigens. In a prospective study based on cold ethanol-fixed mucosal biopsy samples, lesions from 11 ulcerative colitis patients with dysplasia were compared blindly with lesions from 6 patients with reactive hyperplasia and with samples obtained endoscopically from 8 normal controls. The range of disease-associated fluorescence intensity scores was wide. The wide ranges of individual fluorescence scores precluded the possibility of applying carcinoembryonic antigen, secretory component, and epithelial IgA as immunohistochemical markers to differentiate between dysplasia and reactive hyperplasia in routine diagnostic work. (43 Refs)

45. HUMAN PLASMACYTOMA WITH AN UNUSUAL KARYOTYPE GROWING IN VITRO AND PRODUCING LIGHT-CHAIN IMMUNOGLOBULIN.

Karpas A, Fischer P, Swirsky D
Dept. Haematological Medicine, Cambridge Univ. Clinical Sch., Cambridge, England
Lancet; 1(8278):931-933 1982

A new human plasmacytoma line (Karpas 707) was established from the cells of the bone-marrow and peripheral blood of a patient with Bence-Jones-positive multiple myeloma. The cells of this new line resembled the patient's malignant cells and fresh myeloma cells from nine other patients in being Epstein-Barr viral nuclear antigen negative. They looked like plasma cells and they secreted only lambda light chains. Both these cells and the patient's fresh cells were hypodiploid and contained the Philadelphia chromosome and several other markers. This line seems to be the first human plasmacytoma line since the IgE lambda-producing line (U266) established in 1968, and it may be suitable for the production of human monoclonal antibodies. (Author abstract) (14 Refs)

46. COMPARISON OF THE RECEPTORS FOR IGE OF VARIOUS RAT BASOPHILIC LEUKAEMIA CELL LINES. II. STUDIES WITH DIFFERENT ANTI-RECEPTOR ANTISERA.

Froese A, Helm RM, Conrad DH, Iserskey C, Ishizaka T
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Immunology; 46(1):117-123 1982

Receptors for IgE of rat basophilic leukemia (RBL) cells, maintained in different laboratories were isolated by means of various anti-receptor antisera, and characterized by sodium dodecyl sulfate (SDS)-polyacrylamide gel electrophoresis. Most antisera were shown to react with a receptor designated H and which, as shown previously, could be isolated by IgE-Sepharose but not by a combination of IgE and anti-IgE. Only two highly purified anti-receptor antibody preparations, which had been purified by adsorption to and elution from rat basophilic leukemia cells, reacted primarily with a second kind of receptor molecule which had previously been designated R. Some indirect evidence was obtained which suggests that H is a highly immunogenic molecule. It was confirmed that the apparent mol wt of H-like molecules varied on different RBL cell lines. (Author abstract) (11 Refs)

47. COMPARISON OF THE RECEPTORS FOR IGE OF VARIOUS RAT BASOPHILIC LEUKAEMIA CELL LINES. I. RECEPTORS ISOLATED BY IGE-SEPHAROSE AND IGE AND ANTI-IGE.

Froese A, Helm RM, Conrad DH, Isersky C, Ishizaka T, Kulczycki A
M.R.C. Group in Allergy Res., Dept. Immunology, Univ. Manitoba, 730 William Ave., Winnipeg, Man. R3E 0W3, Canada
Immunology; 46(1):107-116 1982

Receptors for IgE of rat basophilic leukemia (RBL) cells, maintained in different laboratories were isolated by means of IgE-Sepharose of IgE and anti-IgE, and characterized by SDS-polyacrylamide gel electrophoresis. All cell lines were found to be associated with a receptor molecule (R) which could be isolated either with IgE-Sepharose or IgE and anti-IgE and a second receptor (H) which could only be isolated with the aid of IgE-Sepharose. The relative amounts of these two molecules as isolated from surface iodinated cells, varied from one RBL cell line to the other and their apparent molecular weights were not identical on all cell lines. Since comparisons were made on the same gel using receptors isolated from cells labeled with different isotopes of iodine, differences in molecular weight must be considered as being intrinsic and not due to methodological variations. These results provide an explanation why differences were observed among receptors for IgE as characterized in various laboratories. In spite of the fact that the various RBL cell lines originated from the same chemically-induced tumor they have, over the years, undergone changes which are reflected in the receptors for IgE. (Author abstract) (27 Refs)

48. STRUCTURE OF GENES FOR MEMBRANE AND SECRETED MURINE IGD HEAVY CHAINS.

Cheng HL, Blattner FR, Fitzmaurice L, Mushinski JF, Tucker PW
Dept. Microbiology, Univ. Texas Southwestern Medical Sch., Dallas, TX, 75235
Nature; 296(5856):410-415 1982

We have sequenced secreted and membrane terminal exons of the murine immunoglobulin delta chain. The putative transmembranal exon is strikingly similar to that of the mu chain and the internal cytoplasmic exon codes for exactly the same two amino acids, valine and lysine. A third potential exon was found between S and M exons that could code for yet another hydrophilic carboxyl terminus termed deltaX. (Author abstract) (46 Refs)

49. WALDENSTROM'S MACROGLOBULINEMIA.

Freixa AA, Ordi Ros J, Mirada Canals A
Departamento de Medicina Interna, Ciudad Sanitaria 'Fracisco Franco', Barcelona, Spain
Rev Clin Esp; 163(3):151-156 1981

Waldenstrom's macroglobulinemia (WM) was discussed, and the following aspects were included physiopathology [formation of B lymphocytes, synthesis of immunoglobulins (Ig), structure of Ig, Ig M, and the concept of clone], relationship between WM and other hematic cancers, clinical aspects (related to proliferation of the B lymphocytes and increased quantities of macroglobulins in blood), diagnosis (results of tests, proteinography, and histologic examination), and treatment (chemotherapy, plasmapheresis, splenectomy, therapy with corticoids, radiotherapy, and others). (37 Refs) (In SPA)

50. ANTIBODY DIVERSITY VERSUS ANTIBODY COMPLEMENTARITY.

Kabat EA
NCI, Bethesda, MD
Pharmacol Rev; 34(1):23-38 1982

The evidence for current views of how antibody combining sites can have so many distinct specificities is reviewed. The sequencing of two kappa Bence Jones proteins from two individuals has shown the existence of variable and constant regions; as heavy chain sequences have been determined, the generally accepted domain theory that ascribes distinct function to each domain has been put forward. Variability at different positions for the variable region of light chains is presented. FR2 sets in mouse and rabbit Vkappa chains and number of chains in each set including those found in human and rabbit Vkappa are listed. (167 Refs)

51. COMPARISON OF SECRETED AND MEMBRANE-BOUND HUMAN IMMUNOGLOBULINS M AND D.

Bijlenga RK, Kocher HP, Jaton JC
Dept. Pathology, Univ. Geneva, CH-1211 Geneva 4, Switzerland
Protides Biol Fluid Proc Colloq; 29:45-48 1982

Structural data obtained with human membrane-bound (u-m) and secreted (u-s) immunoglobulin M heavy chains suggest: (1) u-m has a molecular size slightly larger than u-s, (2) u-m can only be efficiently labeled with a hydrophobic reagent, and (3) amino acids released at the C-termini of the chains are different. Preliminary data on the polypeptide structure of the membrane-bound and intracellular Fc fragments of human IgD suggest that the human delta chain is made up of three constant domains as in human IgD myeloma proteins, in contrast to murine delta chains. (16 Refs)

52. STRUCTURAL STUDIES OF HUMAN IGD.

Debuire B, Putnam FW
Dept. Biology, Indiana Univ., Bloomington, IN, 47405
Protides Biol Fluid Proc Colloq; 29:41-44 1982

Studies on the structure of the human myeloma IgD protein designated WAH are presented. The approach to complete the sequence of the Fd region and of the hinge is to produce large fragments for sequenator analysis by specific chemical cleavage at methionine and tryptophan residues. The fragments were also subjected to secondary cleavage with enzymes such as trypsin and Staphylococcus aureus V8 protease. Besides three glucosamine oligosaccharides (GO) in Fc, three or more GO were found in the hinge. (5 Refs)

53. MOUSE SPLEEN AND IGD-SECRETING PLASMACYTOMAS CONTAIN MULTIPLE IGD DELTA CHAIN RNAS.

Fitzmaurice L, Owens J, Blattner FR, Cheng HL, Tucker PW, Mushinski JF
Lab. Immunology, Natl. Inst. Allergy and Infectious Diseases, NCI, NIH, Bethesda, MD, 20205
Nature; 296(5856):459-462 1982

Fragments of 32P-labelled DNA prepared from a delta cDNA clone and a delta genomic clone, obtained from normal mouse spleens and two gamma messenger RNA (mRNA)-containing, IgD-secreting mouse plasmacytomas TEPC 1017 and TEPC 1033, were used to characterize by hybridization the delta RNAs fractionated on methyl mercury hydroxide agarose gels. Normal mouse spleens contained a major 2.9 kilobase (kb) and a minor 2.1 kb RNA encoding membrane-bound delta chain (gamma-m) RNA plus a 1.75-kb RNA encoding secreting delta chains. Less abundant delta RNA species (2.65 and 3.2 kb) were also observed. Different gene segments or combinations of segments were used in the 3' termini of the multiple delta RNAs. The results indicated that the delta chain is unusual among immunoglobulins in that its mRNA may exist in many forms. Delta RNA in spleen and in TEPC 1017 and TEPC 1033 which encode the membrane forms of delta chain and share certain significant characteristics were identified. Most important, a hydrophobic polypeptide is encoded in both the 2.9-and and the 2.1 kb delta-m mRNA found in the spleen and the plasmacytomas. Implications of the findings are discussed. (35 Refs)

54. FUNCTIONAL ANALYSIS OF HUMAN IA SUBSETS.

Accolla RS, Moretta A, Cerottini JC
Lausanne Branch, Ludwig Inst. Cancer Res., Epalinges, Switzerland
Protides Biol Fluid Proc Colloq; 29:719-722 1982

The role of two distinct human immune region-associated (Ia) subsets, designated NG1 and NG2, which are expressed irrespective of HLA D-locus phenotype, were studied in vitro using the allogeneic mixed WBC reaction. D1-12 and D4-22 monoclonal antibodies were obtained by fusing spleen cells of BALB/c mice and the mouse myelomas Pc-X63-Ag8 (D1-12) and P3-NSI/1 Ag4 (D4-22). When either D1-12 or D4-22 were added to mixed lymphocyte cultures (MLC), the proliferative response was completely abolished. The effect was specific inasmuch as culture fluid from the parental myeloma P3x63 had no inhibitory effect. Titration of the monoclonal antibodies showed that as little as 2.5 ul of D1-12 or 1 ul of D4-22 was sufficient to reduce by 50% the proliferative response of 1 x 10(5) peripheral blood mononuclear cells (PBMC). The MLC response induced by a stimulator cell population which had been treated with anti-Ia Mab and complement (C) was examined. Pretreatment of PBMC with D1-12 and C strongly reduced their capacity to stimulate relevant responder cells in MLC. When PBMC treated with D1-12 and C were used as a source of responder cells, a marked inhibition of the MLC response was obtained, with 3H-thymidine incorporation values never higher than 20% of control values. The results indicated that addition of D1-12 or D4-22 completely inhibits the proliferative response generated in MLC and suggested that Ia structures are present either on responder T cells or on other regulatory cells involved in T cell responses in MLC. (9 Refs)

55. CYANOGEN BROMIDE FRAGMENTS OF MOUSE IGG2A AND IGG2B WHICH BIND TO THEIR FC RECEPTORS ON MOUSE MACROPHAGES.

Diamond B, Campbell R, Schneck J, Birshtein BK
Dept. Microbiology and Immunology, Albert Einstein Coll. Medicine, 1300 Morris Park Ave., Bronx, NY, 10461
Protides Biol Fluid Proc Colloq; 29:415-418 1982

Identification of the portions of mouse IgG2b and IgG2a immunoglobulins recognized by their specific Fc receptors on mouse macrophages was determined with the use of cyanogen bromide fragments. A fragment from the Ch2 domain of IgG2b bound uniquely to the gamma2b Fc receptor while the gamma2a Fc receptor bound two widely spaced fragments, one from the CH2, and one from the CH3 domains. Fragments H-5 and H-10 competed with intact IgG2a protein for binding to the gamma2a Fc receptors. The binding of H-10 augments the binding of the H-5 fragment. The implications of these findings are discussed. (6 Refs)

56. HUMAN IMMUNOGLOBULIN HEAVY CHAIN GENES MAP TO A REGION OF TRANSLOCATIONS IN MALIGNANT B LYMPHOCYTES.

Kirsch IR, Morton CC, Nakahara K, Leder P
Lab. Molecular Genetics, Natl. Inst. Child Health and Human Development, Bethesda, MD, 20205
Science; 216(4543):301-303 1982

A human immunoglobulin heavy chain (gamma4) gene is mapped by chromosome hybridization in situ. This gene is located at band 14q32, a site commonly involved in a chromosomal translocation characteristic of malignant B cells. (Author abstract) (45 Refs)

57. IN VITRO REGULATION OF IMMUNOGLOBULIN SYNTHESIS AFTER HUMAN MARROW TRANSPLANTATION. II. DEFICIENT T AND NON-T LYMPHOCYTE FUNCTION WITHIN 3-4 MONTHS OF ALLOGENEIC, SYNGENEIC, OR AUTOLOGOUS MARROW GRAFTING FOR HEMATOLOGIC MALIGNANCY.

Witherspoon RP, Lum LG, Storb R, Thomas ED
Div. Oncology, Fred Hutchinson Cancer Res. Center, 1124 Columbia St., Seattle, WA, 98104
Blood; 59(4):844-850 1982

Immunoglobulin secretion was studied in 37 patients between 19 and 106 days after allogeneic HLA-identical (30 patients), allogeneic one HLA-haplotype-identical (3 patients), syngeneic (3 patients), or autologous (1 patient) marrow grafting. E rosette-positive (T) and E rosette-negative (non-T) peripheral blood mononuclear cells were cocultured with pokeweed mitogen for 6 days. Polyvalent immunoglobulin secretion was determined by counting plaque forming cells in a reverse hemolytic plaque assay. The number of antibody secreting cells in cocultures of autologous T and non-T lymphocytes was low in 40 of 44 tests conducted on samples from the 37 patients. Mononuclear or non-T cells from 38 of 40 tests failed to produce antibody when cultured with normal helper T cells. T cells from 23 of 37 tests failed to help normal non-T cells secrete antibody. T lymphocytes from 23 of 41 tests suppressed antibody production greater than 80% by normal T and non-T cells. The suppressor cells were radiosensitive in 17 of the 25 tests. The abnormal function of lymphocyte subpopulations in patients during the first 3 mo after syngeneic, allogeneic or autologous marrow grafting was similar regardless of the type of graft or the presence of acute graft vs host disease. (Author abstract) (29 Refs)

58. HETEROZYGOSITY AT GM LOCI ASSOCIATED WITH HUMORAL IMMUNITY TO OSTEOSARCOMA.

Pandey JP, Shannon BT, Tsang KY, Fudenberg HH, Camblin JG
Deppt. Basic and Clinical Immunology and Microbiology, Medical Univ. South Carolina, Charleston, SC, 29425
J Exp Med; 155(4):1228-1232 1982

The possible role of Gm allotypes (genetic markers of IgG) in predisposition to osteosarcoma was investigated. Blood was collected from 50 patients with osteoblastic sarcomas and the presence of osteosarcoma-associated antigens (OSAA) was studied and Gm allotyping was performed. Of the five Gm phenotypes present in the blood, none were significantly associated with osteosarcoma. Two Gm phenotypes (Gm 3;5,13,14 and Gm 1,3,17;5,13,14,21) were significantly associated with immune response to OSAA: the first was associated with no detectable antibody (8% positive and 63% negative) and the second was clearly associated with detectable antibodies to OSAA (83% positive and 11% negative). Since the most probable genotype of the Gm 3;5,13,14 phenotype is Gm 3;5,13,14/Gm 3;5,13,14 and that of Gm 1,3,17;5,13,14,21 is Gm 1,17;21/Gm 3;5,13,14, it was postulated that two Ir genes were in linkage disequilibrium with the Gm 1,17;21 and Gm 3;5,13,14 haplotypes. Possession of either gene alone would not confer humoral responsiveness to OSAA; however, in the heterozygous condition (Gm 1,17;21/Gm 3;5,13,14) the genes would complement to permit a humoral response to OSAA. (23 Refs)

59. MULTIPLE IMMUNOGLOBULIN HEAVY-CHAIN GENE TRANSCRIPTS IN ABELSON MURINE LEUKEMIA VIRUS-TRANSFORMED LYMPHOID CELL LINES.

Alt FW, Rosenberg N, Enea V, Siden E, Baltimore D
Center for Cancer Res., Massachusetts Inst. Technology, Cambridge, MA, 02139
Mol Cell Biol; 2(4):386-400 1982

The immunoglobulin heavy-chain proteins and RNAs produced by a large number of Abelson murine leukemia virus (A-MuLV) transformants were analyzed. A variety of mu (u)-related RNA species and gamma-related species were found in these cells. The productive RNAs were termed Pu-RNA; the aberrant RNAs, Au-RNAs; and the sterile RNAs, Su-RNAs. These three classes of Cu-containing RNA species in A-MuLV transformants were characterized. The data support the concept that heavy-chain allelic exclusion is a consequence of feedback control from cytoplasmic u chains and is not controlled at the DNA or RNA levels. (53 Refs)

60. IMMUNOGLOBULIN ALLOTYPES AND NONSEMINOMA TESTICULAR CANCER.

Ockhuizen T, Pandey JP, Marrink J, Fudenberg HH
Dept. Basic and Clinical Immunology and Microbiology, Medical Univ. South Carolina, Charleston, SC, 29403
Oncology; 39(3):152-155 1982

Gm, A2m, and Km allotypic markers were examined in 52 Dutch patients with nonseminoma testicular cancer. The distribution pattern of the immunoglobulin allotypes in different groups of patients, classified according to histological diagnosis, did not differ significantly from that in the normal population. These results indicate no relationship between nonseminoma testicular cancer and immunoglobulin allotypes. (Author abstract) (19 Refs)

HUMORAL IMMUNE BLOCKING FACTORS AND ANTIGEN-ANTIBODY COMPLEXES

61. THE PRODUCTION OF ANTI-IDIOTYPIC ANTIBODIES AND OF IDIOTYPE-ANTI-IDIOTYPE IMMUNE COMPLEXES AFTER POLYCLONAL ACTIVATION INDUCED BY BACTERIAL LPS.

Rose LM, Goldman M, Lambert PH
(c/o Lambert) World Health Organization Immunology Res. Training Center, Hopital Cantonal, Centre de Transfusion, 1211 Geneve 4, Switzerland
J Immunol; 128(5):2126-2133 1982

BALB/c mice injected with LPS were found to produce anti-Phosphorylcholine (PC) antibodies that had the same idiotype as the BALB/c IgA myeloma protein TEPC-15 (T15 idiotype) as well as anti-idiotypic antibodies directed against the T15 idiotype. Anti-PC plaque-forming cells (PFC) were detected 6 to 12 and 21 to 28 days after injection, whereas anti-T15 idiotype cells (PFC) were detected 3 to 9 and 18 to 21 days after injection of LPS. Immune complexes reacting with conglutinin bound tubes were detected in the circulation 3 days after injection of LPS. Some of the conglutinin-bound complexes were able to bind 125I-TEPC-15 myeloma protein, but not 125I-HPC-16, a BALB/c monoclonal IgM anti-PC antibody that does not bear the T15 idiotype. In addition, these complexes did not bind 125I-MOPC-167 or 125I-MOPC-315, two other BALB/c myeloma proteins that do not bear the T15 idiotype. Prior exposure to PC antigenic determinants enhances both the anti-PC response and the anti-T15 idiotype response. In addition, priming may influence the expression of other anti-idiotypic clones. Immune complexes from PC-KLH-primed mice were able to bind 125I-HPC-16 monoclonal antibody, but not 125I-MOPC-167, another PC-binding BALB/c myeloma protein that does not bear the T15 idiotype. These results demonstrate that the polyclonal B cell activation induced in vivo by LPS stimulates the simultaneous production of antibodies bearing the T15 idiotype and of corresponding anti-T15 idiotype antibodies. These two antibody populations were found to form complexes and to persist in the circulation for an extended period of time. These results suggest that the induction of polyclonal antibody synthesis that occurs in a variety of infectious and autoimmune diseases may (1) induce profound changes in idiotypic interactions within the B cell repertoire and (2) be responsible for the high incidence of immune complexes in these diseases. (Author abstract) (39 Refs)

62. HEPATOBILIARY TRANSPORT OF IGA IMMUNE COMPLEXES: MOLECULAR AND CELLULAR ASPECTS.

Brown TA, Russell MW, Mestecky J
Dept. Microbiology and Inst. Dental Res., Univ. Alabama in Birmingham, Birmingham, AL, 35294
J Immunol; 128(5):2183-2186 1982

The molecular and cellular parameters of the transport of IgA immune complexes (IgA-IC) from the circulation to the bile in vivo were studied in mice. Polymeric MOPC 315 IgA was effective in the transport of 125I-DNP-HSA into the bile, whereas complexes containing monomeric IgA were not transported. The transport of IgA-IC could be blocked by excess free IgA of different antigen specificity, but not by IgG or IgM. Hepatobiliary transport did not appear to involve the galactose- or mannose-specific glycoprotein receptors of the liver. No difference in IgA-IC transport, relative to controls, could be seen in mice that had been treated with cobra venom factor or whose mononuclear phagocytic system had been blockaded with colloidal carbon. These data suggest that the hepatobiliary transport of IgA-IC proceeds by a mechanism similar to the selective transport of free polymeric IgA through the hepatocyte. (Author abstract) (30 Refs)

63. IMMUNOCOMPLEXES AND PRIMARY LUNG CANCER.

Lenzini L, Rottoli L, Sestini P, Carriero G, Sani G, Gotti G

Istituto di Tisiologia e di Malattie dell'Apparato Respiratorio, Università degli Studi di Siena, Via Tufi, 1, Siena, Italy

Allergol Immunopathol (Madr); 9(2):119-122 1981

Circulating immune complexes (CIC) were studied in a selected group of 71 patients (66 males, 5 females; aged 44-71 yr) with a histologic diagnosis of primary lung cancer (PLC). Histologic types included 49 epidermoid carcinomas, 13 adenocarcinomas, and 9 anaplastic small cell carcinomas. With regard to TNM staging, 21 were Stage I, 9 Stage II, and 41 Stage III. Assay of CIC was performed by precipitation of sera in polyethylene glycol, and the C1q, IgG and IgM fractions were measured by simple radioimmunodiffusion. Sera with at least one of the three fractions was considered positive; by this method CIC were found in 47% of the 71 patients before treatment. Statistically significant elevations of CIC were found in patients with epidermoid carcinoma: 3/15 in stages I and II, and 20/34 in stage III. CIC showed a significant tendency to increase with progression of clinical stage. Analysis of CIC behavior in comparison with single fractions showed that C1q and/or IgG were elevated in 40% of the patients. Presence of C1q and/or IgG associated with IgM was more characteristic of Stage N2 while C1q and/or IgG not associated with IgM was more frequent in Stage N1. In 20 patients who underwent radical surgery, a higher rate of metastasis was found in those with elevated CIC before surgery. Survival rate 12 mo after the first examination was significantly lower in 33 patients with elevated CIC compared to 38 patients who were negative. (15 Refs)

64. IMMUNE COMPLEXES IN OVARIAN CANCER.

Clayton LA, Gall SA, Dawson JR, Creasman WT

Div. Gynecologic Oncology, Dept. Obstetrics and Gynecology, Duke Univ. Medical Center, Durham, NC, 27710

Gynecol Oncol; 13(2):203-212 1982

A polyethylene glycol precipitation (PEG) assay has been used to identify immune complexes in the serum of patients with ovarian cancer. Single radical immunodiffusion was used to quantitate the amount of IgG contained in the immune complexes. This study has shown that significantly higher levels of immune complexes were detected in the serum of ovarian cancer patients with known tumor when compared with ovarian cancer patients who were in remission. Values obtained for patients in remission were within the range of the control group. The levels of immune complexes were also noted to rise before the clinical detection of recurrences or progression of disease. It is therefore suggested that the PEG assay may be a useful marker in patients with ovarian cancer. (Author abstract) (25 Refs)

HUMORAL IMMUNOSUPPRESSIVE AGENTS

65. THE MECHANISM OF IMMUNOSUPPRESSION IN TUMOR-BEARING MICE: DIFFERENT SUSCEPTIBILITY OF VARIOUS IMMUNE RESPONSES TO IMMUNOSUPPRESSION AND MACROPHAGE SERIES AS TARGETS FOR IMMUNOSUPPRESSION.

Okuda S

Dept. Immunology, Dept. Internal Medicine, Faculty Medicine, Kyushu Univ., Fukuoka 812, Japan

Fukuoka Igaku Zasshi; 72(12):687-702 1981

Immunosuppression was investigated in thymic lymphoma (EL-4)-bearing C57BL/6 mice immunized with chicken red blood cells (CRBC). Corynebacterium parvum was used as macrophage activating agent. After a primary immunization with CRBC, production of antibody, cell mediated cytotoxicity (CMC), and delayed type footpad reaction (DFR) were suppressed; soon thereafter the reactions, except for DFR, were restored despite enlargement of the tumor. After a secondary immunization, only DFR was suppressed. Before immunization, the introduction of serum taken from the tumor-bearing mice suppressed production of antibody slightly but strongly suppressed CMC and DFR; after immunization, only DFR was suppressed. The effect of transfer of spleen cells taken from tumor-bearing mice with secondary immunization on DFR was similar to that of transfer of spleen cells taken from similarly immunized normal mice. No DFR was induced with spleen cells taken from primary immunized tumor-bearing mice. The administration of C parvum restored the production of antibody, CMC, and DFR. In the secondary immunized tumor-bearing mice, administration of C parvum restored DFR but had no effect on production of antibody and CMC. DFR was restored with C parvum treatment in the tumor-bearing mice adoptively transferred with spleen cells taken from immunized DFR positive mice. Only the group of spleen cells from which cells adhering to the glass petri dish had been removed lost the ability to restore the suppressed immune reaction. In vitro experiments showed that accessory cell function of adherent cells was impaired in the tumor-bearing mice and treatment with C parvum restored the function. When serum obtained from the tumor-bearing mice was fractionated by Sephadex G-200, the fraction containing molecules with relatively high mol wt exhibited immune suppression ability. The results suggest that immune suppression may be the result of lowered accessory cell function of macrophages and suppression of macrophages as the secondary cell in FDR. C parvum seems to restore both functions by stimulating macrophages. (58 Refs) (In JPN)

66. THE ROLE OF IMMUNOSUPPRESSANTS IN LYMPHOCYTE FUNCTION.

Winkelstein A

Dept. Medicine, Montefiore Hosp., Pittsburgh, PA, 15213

The Handbook of Cancer Immunology Volume 6: Lymphoid Cell Subpopulations-Structure, Function, and Interactions. Waters H, ed. New York, Garland STPM Press, 314 pp., 1981.

Effects of cytotoxic drugs on lymphocyte numbers, functional activities, and immunosuppressive properties are discussed. Such effects are closely correlated with the drugs' cell cycle specificities. Specific agents discussed include azathioprine, cyclophosphamide, methotrexate, and chlorambucil. Humoral and cell-mediated responses, toxicities, and use of corticosteroids are considered. (128 Refs)

67. IMMUNOSUPPRESSIVE EFFECT OF MOUSE SERUM LIPOPROTEINS. II. IN VIVO STUDIES.

Hsu KH, Hiramoto RN, Ghanta VK
(c/o Hiramoto) Dept. Microbiology, Univ. Alabama Birmingham, University Station, Birmingham, AL, 35294
J Immunol; 128(5):2107-2110 1982

Normal mouse serum lipoproteins suppress a number of immunologic functions, such as mitogen stimulation, primary immune response, and allograft rejection in vivo. The effects of one class of lipoproteins, high density lipoprotein (HDL), were investigated after iv administration. Max suppression of spleen and peripheral blood lymphocyte (PBL) mitogen stimulation occurred when HDL was administered up to 8 hr before testing. Spleen cells remained suppressed 48 hr after injection, while PBL regained most of their activities. Injection of HDL 24 hr after sheep red blood cell (SRBC) immunization was as effective as giving HDL 8 hr before SRBC in suppressing primary immune response to SRBC. Induction of T cell allograft immunity was also suppressed by the injection of HDL. (Author abstract) (25 Refs)

68. MITOGEN-INDUCED BLASTOGENESIS AND RECEPTOR MOBILITY INHIBITION BY BREAST CANCER SERUM WITH ELEVATED OROSOMUCOID (ALPHA1-ACID GLYCOPROTEIN) LEVELS.

Cheresh DA, Distasio JA, Vogel CL, Lopez DM
(c/o Distasio) Dept. Microbiology D4-4, Univ. Miami Sch. Medicine, P.O. Box 016960, Miami, FL, 33101
JNCI; 68(5):779-783 1982

Sera from cancer patients have been shown to suppress normal lymphoid cell responsiveness in vitro. In the present study, sera from breast cancer patients were demonstrated to be inhibitory to the concanavalin A (Con A)-, Proteus vulgaris-derived phytohemagglutinin-, and pokeweed mitogen-induced blastogenic responses of normal lymphoid cells. Orosomucoid (OR) (alpha1-acid glycoprotein), an acute-phase reactant, was elevated in these sera, and a positive correlation existed between the OR level in the sera and its immunosuppressive capacity. When normal lymphoid cells were reacted in fluorescein isothiocyanate-labeled Con A, cells that had been preincubated in breast cancer sera known to contain an elevated level of OR showed a significant decrease in Con A receptor mobility as compared to the receptor mobility of the same lymphoid cells preincubated in normal sera. Thus a component(s) from the sera of breast cancer patients had the capacity to inhibit lymphocyte activation. This inhibition might have resulted from an interaction of OR with the cell membrane. (Author abstract) (34 Refs)

69. IMMUNOSUPPRESSIVE EFFECT OF ANTILYMPHOCYTIC SERUM ON EXPERIMENTAL GIARDIASIS - A PILOT STUDY.

Aggarwal A, Bhatia A, Vinayak VK
(c/o Vinayak) Dept. Experimental Medicine, Postgraduate Inst. Medical Education and Res., Chandigarh 160012, India
Indian J Med Res; 74:840-844 1981

Swiss albino mice immunodepressed with rabbit antimouse antilymphocytic serum (ALS) or exposed to whole body irradiation, challenge upon intra-esophageally with Giardia lamblia cysts, had higher cysts excreted in feces in 2 hr collection and also had high trophozoite counts in the duodenum at various stages of observation, as opposed to control animals. The cysts excreted by animals exposed to whole body irradiation reached a low level by 31 +-2 days as against 51 +-5 days among ALS treated animals while in control animals the similar level was achieved by 23 +-3 days. ALS treated animals underwent a spontaneous resolution of infection by 62 +-5 days while in control group it was achieved by 48 +-5 days. There was no significant change in the wt of animals in any group during the period of observation and there was also no morbidity or mortality. It is inferred that the immune mechanisms at cellular level play a significant role in the continuation of G lamblia infection. (Author abstract) (18 Refs)

70. REVERSAL BY CITROVORUM FACTOR OF METHOTREXATE-INDUCED SUPPRESSION OF CELL-MEDIATED AND HUMORAL IMMUNE RESPONSE IN MOUSE MODEL SYSTEMS.

Bogyo D, Ehrke MJ, Mihich E
(c/o Mihich) Dept. Experimental Therapeutics, Roswell Park Memorial Inst., Buffalo, NY, 14263
Biochem Pharmacol; 31(7):1387-1392 1982

C3H/HeHa mice were immunized (day 0) with 5 x 10(8) sheep red blood cells (SRBC) or 3 x 10(7) EL-4 lymphoma cells (ip), and C57Bl/6J mice were immunized (day 0) with 3 x 10(7) P815 mastocytoma cells (ip). Methotrexate (MTX, 100 mg/kg) was given ip on day +2, with or without citrovorum factor (CF) at equimolar dose. In the absence of CF in C57Bl/6J mice, the complement-independent cellular cytotoxicity (CICC) response did not recover in 18 days from MTX suppression to levels seen in immunized controls, while in C3H mice, with EL-4 as antigen, the response equalled that of controls by day 18 and was similar to or greater than that of controls through day 28; in both cases the serum antibody response returned to control levels by day 20. In both mouse strains, CF produced immediate recovery of the responses measured. In contrast, with SRBC as antigen, while the MTX suppression of complement-dependent cellular cytotoxicity (CDCC) in the absence of CF recovered by day 7, the CICC response recovered much more slowly. CF administration produced a rapid (day 4) return of CDCC activity to control levels, but only a partial restoration of CICC activity by day 6. In conclusion, the kinetics of recovery of the CICC and CDCC responses and of CF rescue of MTX-induced immunosuppression were dependent on mouse strain and on immunogens used, as well as on the type of response measured. Thus, selectivity of MTX action is indicated. (Author abstract) (25 Refs)

71. THE ROLE OF T,B AND ADHERENT CELLS IN THE IN VITRO IMMUNE RESPONSE OF TEPC-183-BEARING MICE.

Patel M, Havas HF
(c/o Havas), Temple Univ. Sch. Medicine, 3400 N. Broad St., Philadelphia, PA, 19140
Immunology; 46(1):97-105 1982

In order to analyze the mechanism of immunosuppression of plasmacytoma-bearing mice, the role of enriched T cells, B cells, and adherent cells from the spleens of normal and TEPC-183 plasmacytoma (IgM,k) bearing mice in the primary in vitro immune response was investigated. Nylon-wool-enriched fractions of T and B cells were used in the study of T-cell-dependent immune responses to the 2-4-6-trinitrophenyl ligand. The data suggest that the suppressed state of TEPC-183 spleen cells may be due to defective T-B cell interaction. It was consistently observed that splenic adherent cells from TEPC-183-bearing mice were neither suppressed nor suppressive for the in vitro immune responses of normal splenic lymphocytes at the ratios tested. The suppressive characteristic of adherent PE cells in this system is not specific for TEPC-183 plasmacytoma in mice. The possible role of esterase-positive cells, T cells, B cells, and adherent cells in the observed suppression will be discussed. (22 Refs)

72. A CLONED T-CELL LINE FROM A TOLERANT MOUSE REPRESENTS A NOVEL ANTIGEN-SPECIFIC SUPPRESSOR CELL TYPE.

Heuer J, Bruner K, Opalka B, Kolsch E
Dept. Immunology, Univ. Munster, Domagkstrasse 10, 4400 Munster, W. Germany
Nature; 296(5856):456-459 1982

Two major alternative models, clonal deletion and suppression, have been proposed as possible explanations for immunological tolerance. We have now isolated a functional T suppressor (Ts) cell clone to analyze the role of Ts cells in the induction and maintenance of tolerance. This cloned, long-term cultured Ts cell line (HF1) was derived from CBA/J mice (H-2k) in which low-zone tolerance (LZT)(3) had been induced by subimmunogenic doses of bovine serum albumin (BSA). HF1 cells show BSA-specific suppressor activity in two in vitro suppressor assays. HF1 Ts cells and a factor derived from them suppress unprimed, carrier-specific T helper (Th) cells in an assay measuring IgG antibody production against fluorescein-conjugated BSA (Flu-BSA). Furthermore, they block DNA synthesis in an antigen-specific in vitro T-cell proliferation assay. Their proliferation in the presence of antigen-presenting cells is antigen specific and shows restriction to the I-Ak region of the major histocompatibility complex (MHC). In addition, HF1 Ts cells have a characteristic cytotoxic activity. The data reported suggest that clonal deletion and suppression models are not necessarily mutually exclusive. Clonal deletion could manifest itself by the action of Ts cells. (Author abstract) (21 Refs)

73. AGE-DEPENDENT SEPARATION OF CLASS-SPECIFIC SUPPRESSOR CELLS IN THYMUS OF SJL/J MICE.

Clark DA, Cinader B, Koh SW
Dept. Medicine, McMaster Univ., Hamilton, Ontario L8N 3Z5, Canada
Immunol Lett; 3(4):189-194 1981

Thymocytes from young SJL/J mice (3-6 wk) contain suppressor cells that inhibit the antibody response of lymph node cells to sheep RBC. Effect of these suppressor cells disappears at age 24 wk or more. These aged animals acquire thymic suppressor cells which suppress the generation of cytotoxic T-cells, both in vivo and in vitro. While such suppressors are not present in the thymuses of young mice, suppression can be induced with estrogen and progesterone. The differentiation of functionally different suppressor cell populations in thymus may be affected by both age and hormonal status. (37 Refs)

74. T LYMPHOCYTE-MEDIATED SUPPRESSION OF MYELOMA FUNCTION IN VITRO. IV. GENERATION OF EFFECTOR SUPPRESSOR CELLS SPECIFIC FOR MYELOMA IDICTYPES.

Abbas AK, Takaoki M, Graene MI
Dept. Pathology, Harvard Medical Sch., Boston, MA, 02115
J Exp Med; 155(4):1216-1221 1982

BALB/c mice were injected iv with viable syngeneic splenocytes to which affinity-purified M315 IgA was coupled developed suppressor T cells (Ts1) that inhibited IgA plaque-forming cells (PFC) after greater than 2 days in culture. On the other hand, T cells induced by soluble extracts of Ts1 cells (TsF1) and sc immunization suppressed greater than 50% of the PFC within 1 day and 80-90% by day 4. The cells mediating rapid suppression were operationally termed effector Ts. The specificity of the effector Ts was assessed by their ability to bind to different myeloma proteins. Suppressive activity was depleted by absorbing effector Ts on dishes coated with M315 IgA but not on dishes coated with MPC11 (IgG2b,k of unknown specificity) or M460 proteins. M315-specific effector Ts did not inhibit MPC 11 cells and caused greater than 70% selective suppression of IgA secretion by the MOPC 315-MPC11 somatic cell hybrid. Effector Ts were Thy-1.2+, Lyt-1-2+ cells, while Ts1 were either Lyt-1+2+ or T lymphocytes bearing both Lyt-1+ and Lyt-2+ markers were necessary for Ts1 to induce or mature into effector Ts in vitro. The ability to induce two cell types at different stages of a suppressor pathway, and to measure their effects on a monoclonal, autonomous target, should facilitate analysis of the differentiation and mechanisms of action of suppressor T lymphocytes. (11 Refs)

75. DIAGNOSIS OF CARCINOMA OF THE PANCREAS BY ASSAY OF IMMUNOSUPPRESSIVE ACIDIC PROTEIN.

Matsuno S, Kobari M, Matsuda Y, Sato T
First Dept. Surgery, Tohuku Univ. Sch. Medicine, Sendai 980, Japan
Tohoku J Exp Med; 136(1):1-10 1982

Immunosuppressive acidic protein (IAP) was measured by single radial immunodiffusion in serum from 46 pancreatic cancer patients, 211 controls, and patients with other malignant or benign inflammatory pancreatic diseases. A normal value of serum IAP of less than 500 ug/ml was used because 194/211 (91.9%) of the controls were below this value. Elevated serum IAP levels were seen in 44/46 (96%) pancreatic cancer patients, 24/26 (92%) bile duct cancer patients, all duodenal papilla or gallbladder cancer patients, 19/29 (66%) of chronic pancreatitis patients, all of acute pancreatitis or pancreatic cyst patients, and 0/3 insulinoma patients. Serum IAP correlated with tumor size and metastatic involvement of the liver and peritoneum, but not infiltration of the pancreatic capsule. It also seemed to correlate with recurrence after surgery, but not with serum carcinoembryonic antigen (CEA) levels, which were elevated (greater than 2.5 nanog/ml) in only 26/46 (57%). Portal blood sampling in four patients did not show elevated IAP or CEA levels at the site of tumor. The value of this assay for screening for pancreatic cancer is discussed. (10 Refs)

OTHER RELATED STUDIES

76. A DIFFERENTIATION ANTIGEN EXPRESSED SELECTIVELY BY A PROPORTION OF HUMAN BLOOD CELLS: DETECTION WITH A MONOCLONAL ANTIBODY.

Brooks DA, Bradley J, Zola H
(c/o Zola) Dept. Clinical Immunology, Flinders Medical Centre, Bedford Park 5042, Australia
Pathology; 14(1):5-11 1982

A monoclonal antibody, FMC 8, has been prepared after immunization with a cell line of the non-T-non-B type acute lymphoblastic leukemia (ALL). The antigen detected by this antibody consists of a single polypeptide chain with an apparent mol wt of 24,000 d. The antigen is absent from T cells but appears after mitogen stimulation. It is found on the majority of normal circulating B cells but is absent in most chronic lymphocytic leukemias. All cells of the non-T-non-B type express the antigen, whereas T-ALL cells generally do not. Granulocytes, monocytes and platelets react with the antibody, but erythrocytes do not. The wide but selective distribution of the antigen renders FMC 8 potentially useful, together with other monoclonal antibodies, in the delineation of differentiation pathways and in phenotypic analysis of leukemia and lymphoma cells. (Author abstract) (28 Refs)

77. THE HANDBOOK OF CANCER IMMUNOLOGY. VOLUME 6: LYMPHOID CELL SUBPOPULATIONS: STRUCTURE, FUNCTION, AND INTERACTIONS.

Waters H
NIH, Bethesda, MD
The Handbook of Cancer Immunology. Volume 6: Lymphoid Cell Subpopulations: Structure, Function, and Interactions. New York, Garland STPM Press, 314 pp., 1981.

Lymphoid cell subpopulations are discussed in relation to cellular interactions in metastasis, role of immunosuppressants in lymphocyte function, human T cell subclasses with IgG and complement receptors, age-related changes in marrow stem cells, functions of atypical lymphocytes, biology of marrow-dependent cells in mice, pathogenesis of plasma cell tumors, functional stimulation of T cells with protein antigens, effects of lymphokines on tumor cells, and perspectives of lymphocyte production and cellular traffic in the bone marrow. (1334 Refs)

78. MACROPHAGE RECOGNITION OF COMPLEMENT-COATED LYMPHOBLASTOID CELLS.

Gomez F, Kelley M, Rossman MD, Dauber J, Schreiber AD
(c/o Schreiber) Hematology-Oncology Section, Hosp. Univ. Pennsylvania, 3400 Spruce St., Philadelphia, PA, 19104
J Reticuloendothel Soc; 31(3):241-249 1982

We utilized an in vitro model to evaluate the recognition of Raji lymphoblastoid cells by human macrophages. Using this model and human IgM anti-Raji antibody, we observed that Raji-macrophage interaction was enhanced by complement activation. Raji-macrophage interaction was dependent upon the number of complement (C1) fixing sites generated per Raji. Pulmonary alveolar macrophages appeared more effective than autologous monocytes in enhancing the recognition of both complement-coated Raji and complement-coated erythrocytes. Pulmonary alveolar macrophages, but not blood monocytes, obtained from smokers were defective in this recognition process. Such pulmonary macrophage dysfunction may contribute to the observed increased incidence of pulmonary infection and neoplasm in smokers. (Author abstract) (24 Refs)

79. ESTABLISHMENT AND CHARACTERIZATION OF HUMAN NEUROBLASTOMA AND GANGLIONEUROBLASTOMA CELL LINES.

Morrison LJ, Cochran AJ, Gibson AA, Willoughby ML, More IA
Dept. Pathology and Surgery, Univ. California Los Angeles Center for Health Sciences, Los Angeles, CA, 90024
Br J Cancer; 45(4):531-542 1982

The establishment in culture and characterization of four human neuroblastoma (NB) cell lines and one human ganglioneuroblastoma cell line are described. Each cell line fulfilled at least two of four criteria for malignant or transformed cells: viz, subcultured more than 70x, high saturation density with absence of contact inhibition, population-doubling time within a range of 10-40 hr, and tumor formation in nu/nu mice. Each cell line also fulfilled at least two of three criteria for neuroblastoma cells: viz, humoral and cell-mediated immune reactivity toward NB-associated cell-surface antigen, intracellular storage and extra-cellular secretion of catecholamines, and characteristic neuroblast and ganglion-cell morphology. (Author abstract) (22 Refs)

80. MONOCLONAL ANTIBODIES THAT RECOGNIZE DISCRETE FORMS OF TUBULIN.

Gozes I, Barnstable CJ
Lab. Neural and Endocrine Regulation, Massachusetts Inst. Technology, Dept. Nutrition and Food Science, Cambridge, MA, 02139
Proc Natl Acad Sci USA; 79(8,part1):2579-2583 1982

Anti-tubulin antibodies secreted by plasmacytoma NSI-spleen cell hybrids were detected by an indirect binding assay. Different antibodies bound to different combinations of the tubulins as resolved by isoelectric focusing. Two monoclonal antibodies (TUB 2.1 and TUB 2.5) labeled only (i) the tubulin band on a polyacrylamide electropherogram and (ii) beta-tubulins as resolved by isoelectric focusing. The fraction that was specifically bound and eluted from antibody affinity columns was enriched in beta-tubulins as compared with alpha-tubulins, suggesting the possibility of some soluble tubulin homodimers and alpha, beta-heterodimers. Double labeling experiments were used to show that all detectable microtubules contained beta-tubulin. (Author abstract) (35 Refs)

81. MONOCLONAL HUMAN B LYMPHOMA CELLS RESPOND BY DNA SYNTHESIS TO ANTI-IMMUNOGLOBULINS IN THE PRESENCE OF THE TUMOUR PROMOTOR TPA.

Godal T, Henriksen AA, Ruud E, Michaelsen T
Lab. Immunology, The Norwegian Radium Hosp., Montebello, Oslo 3, Norway
Scand J Immunol; 15(3):267-274 1982

Monoclonal human B lymphoma cells were triggered in vitro to DNA synthesis with F(ab')2 fragments of rabbit IgG antibodies specific for different human immunoglobulin (Ig) light and heavy chains. The specificity of the responses corresponded to surface Ig (sIg) present on tumor cells. Anti-mu chain, anti-delta chain, anti-gamma chain, and antibodies to light chains were found to mediate this effect. However, to induce DNA synthesis, the tumor promotor 12-O-tetradecanoyl-phorbol-13-acetate (TPA) was usually required. TPA alone induced cytoplasmic protrusions and increases in cellular volume. These observations should provide new opportunities to study the triggering of B cells with anti-Ig in well-defined cell populations. (Author abstract) (33 Refs)

82. NATURAL ANTI-LYMPHOMA ACTIVITY IN C57BL/6 MICE: TIME COURSE OF APPEARANCE AND NATURE OF CYTOTOXIC ANTIBODIES.

Rubio N
Instituto de Immunologia y Biologia Microbiana, Velazquez 144, Madrid 6, Spain
Immunol Lett; 3(4):195-198 1981

The presence of cytotoxic antibodies in the sera of normal C57BL/6 mice was measured by the cytotoxicity test against syngeneic leukemic cells induced by endogenous radiation leukemia virus. Activity could be detected in sera from 5-14-mo-old mice. Study of the nature of the antibody response indicated the activity could be attributed mainly to IgM antibodies until the age of 10 mo, whereas in sera of 12-mo-old mice an increasing level of IgG-like antibodies was demonstrated. (16 Refs)

83. INDUCTION OR ELIMINATION OF TUMOR-SPECIFIC IMMUNITY AGAINST A CHEMICALLY-INDUCED RAT TUMOR USING AUTO-ANTI-IDIOTYPIC IMMUNITY.

Binz H, Meier B, Wigzell H
Inst. Immunology and Virology, Univ. Zurich, CH-8028 Zurich, Switzerland
Int J Cancer; 29(4):417-423 1982

DA rat sarcomas P1 and P2 were induced by dimethylbenz(a)anthracene. A tumor-specific immune response of DA rats against P1-tumor cells could be demonstrated at the humoral and cellular level. DA anti-P1 antibodies were purified on fixed P1-tumor cells and used as autoimmunogen in DA rats for the production of anti-idiotypic antibodies. Such anti-idiotypic antibodies could be demonstrated by using a solid-phase radioimmunoassay and by their ability to induce secondary type of DA anti-P1 responses in vitro. In addition, such antibodies were able to induce cytotoxic T lymphocytes capable of eliminating P1-tumor cells but not control tumor cells. In some of the auto-immunized DA rats enhanced P1-tumor growth could be observed, indicating that the anti-idiotypic immune response had led to a selective ablation of idiotypic, potential anti-P1 reactive T cells. (Author abstract) (30 Refs)

84. MONOCLONAL ANTIBODIES AGAINST UNIQUE I-REGION GENE PRODUCTS EXPRESSED ONLY ON MATURE FUNCTIONAL T CELLS.

Hiramatsu K, Ochi A, Miyatani S, Segawa A, Tada T
Dept. Immunology, Faculty Medicine, Univ. Tokyo, Bunkyo-Ku, Tokyo 113, Japan
Nature; 296(5858):666-668 1982

Mouse T-cell hybrids were developed which produce antigen-specific augmenting and suppressor factors with immune response (I) region-/encoded determinants. A hybridoma produced by fusion of mouse spleen cells with BALB/c mouse plasmacytoma produced monoclonal antibodies against these determinants, which are products of the I-A subregion. These determinants appear to be different from conventional Ia antigens of B cells and macrophages, since none of the monoclonal antibodies reacted with these cell types. The I-A subregion apparently carries genes which are selectively expressed on augmenting and helper T cells. (16 Refs)

85. A RAT MONOCLONAL ANTIBODY AGAINST MOUSE ALPHA AND BETA INTERFERON OF ALL MOLECULAR WEIGHT SPECIES.

Mannel D, De Maeyer E, Kemler r, Cachard A, De Maeyer-Guignard J
Inst. Curie, Centre Universitaire, 91405 Orsay Cedex, France
Nature; 296(5858):664-665 1982

A LOU strain rat was immunized with interferon (IFN) purified from cultures of Swiss mouse C-243 cells which had been infected with Newcastle disease virus. Spleen and mesenteric lymph node cells from the immunized rat were fused with LOU-derived 21ORCY3-Ag1.2.3 rat myeloma cells. The resulting hybridoma secreted monoclonal antibody of the IgG class, with binding activity to all the different mol wt species, as demonstrated by an enzyme-linked immunosorbent assay and by affinity chromatography of a crude INF preparation on columns containing bound anti-IFN antibodies. The antiviral activity of all the mol wt species was neutralized by the antibody but the neutralizing activity was much weaker than the binding activity, indicating the presence of a common antigenic site for all mouse alpha and beta IFN species. (18 Refs)

86. THE INFLUENCE OF ANTIGEN DENSITY AND A COMPARISON OF IGG AND IGM ANTIBODIES IN THE ANTI-COMPLEMENTARY MODULATION OF LYMPHOCYTIC SURFACE IMMUNOGLOBULIN.

Gordon J, Anderson VA, Robinson DS, Stevenson GT
Lymphoma Res. Unit, Tenovus Res. Lab., Southampton General Hosp., Tremona Road, Southampton SO9 4XY, England
Scand J Immunol; 15(2):169-177 1982

Experiments were carried out to determine the influence of antigen density on anti-complementary modulation, defined here as the conferring by anti-immunoglobulin (Ig) of resistance to lysis of guinea pig L2C leukemic lymphocytes through anti-Ig plus syngeneic complement (C). Populations of leukemic cells varied widely in their quantitative expression of surface membrane Ig as judged by the binding to cells of 125I-labeled Fab' fragments from anti-Ig, and a good correlation between the bulk antigen density and the percentage of cells lysed by anti-Ig plus C was obtained ($p = 0.02$). In the presence of 10 mM sodium azide, which has been shown to diminish the modulation occuring during simultaneous incubations with anti-Ig and C, this correlation was even stronger (p less than 0.001). No zone could be defined in which the level of surface Ig expression was sufficient to serve complement lysis but too low for modulation. Furthermore, both the degrees and rates of modulation occurring on incubation with antibody at 37 C, either before C addition or in the presence of lytic C, were similar for populations of high, low, or intermediate antigen density. Separation of cells by their size or density failed to yield populations differing in either their susceptibility to humor killing through anti-Ig or their modulating capacity. IgG and IgM antibodies to the L2C cell surface Ig evoked similar levels of killing with syngeneic C, and when compared for their ability to promote anti-complementary modulation, no difference was revealed in either the rate or degree of modulation occurring during incubations at 37 C with the two isotypes. The findings are discussed with particular reference to observations on the modulation of mouse thymus leukemia (TL) antigens. (Author abstract) (38 Refs)

87. ERADICATION OF BOVINE LEUKEMIA VIRUS INFECTION FROM A HIGH-PREVALENCE HERD, USING RADIOIMMUNOASSAY FOR IDENTIFICATION OF INFECTED ANIMALS.

Ferrer JF
Section Viral Oncology, Comparative Leukemia Studies Unit, Sch. Veterinary Medicine, Univ. Pennsylvania, New Bolton Center, Kennett Square, PA, 19348
J Am Vet Med Assoc; 180(8):890-893 1982

Radioimmunoassay (RIA), using the virion glycoprotein antigen, was applied in an attempt to eradicate bovine leukemia virus (BLV) infection from a herd in which virtually all the adult cattle are infected. Considering that most calves born to BLV-infected cows are negative for BLV at birth and remain negative for the first several mo of life, the eradication program was based on the identification and isolation of the BLV-free calves born to infected cows. Twenty-five calves raised on colostrum and milk from their infected dams were classified as BLV-free on the basis of negative results in the RIA at 6 to 8 and 9 to 11 mo of age. These animals were maintained in either complete (10 calves) or partial (15 calves) isolation from infected cattle and were examined at regular intervals for BLV and BLV antibodies. With the exception of one calf in the group raised in partial isolation, the animals have remained free of BLV up to the time of the last evaluation, when they were 32 to 35 mo old. At these ages, more than 90% of the nonisolated cattle in the herd are BLV-positive. The data also show that this eradication trial would have failed if in the initial procedure used to classify the calves as BLV-free, the agar gel immunodiffusion test instead of the RIA had been used. Inasmuch as the 25 calves in this study were fed colostrum and milk from their dams, the fact that only 1 of the calves became infected during the 26 to 29 mo of observation provides further evidence that milk-borne transmission of BLV is infrequent and perhaps inconsequential. (Author abstract) (32 Refs)

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TUMOR ANTIBODY PRODUCTION/ CHARACTERIZATION/ DETECTION

1. IN VITRO PRODUCTION OF TUMOR-RELATED HUMAN MONOCLONAL ANTIBODY AND ITS IMMUNOHISTOCHEMICAL SCREENING WITH AUTOLOGOUS TISSUE.

Hirohashi S, Shimosato Y, Ino Y
Pathology Div., Natl. Cancer Center Res. Inst., 1-1, Tsukiji 5-chome, Chuo-ku, Tokyo 104, Japan
Gan; 73(2):345-347 1982

The property of Epstein-Barr virus (EBV) to transform human B lymphocytes into lymphoblastoid cells secreting immunoglobulins was used to obtain human antibodies against human tumors. EBV was taken from the marmoset cell line B95-8. A virus stock was produced by culturing B95-8 cells for 7 days in a medium of RPMI-1640 supplemented with 20% heat inactivated fetal bovine serum, 100 Units/ml penicillin, and 100 ug/ml streptomycin, separating culture supernatants, and filtering through a Millipore filter. Regional lymph nodes were obtained at surgery from a 45-yr-old woman with Dukes' C moderately-differentiated adenocarcinoma of the rectum and

HE 20.3173/2:

from a 37-yr-old man with Borrmann's Type II signet ring cell carcinoma of the stomach. Single cell suspensions were prepered from the lymph nodes, resuspended in culture medium, and then mixed with virus stock. A 0.1 ml portion of the resulting mixture was distributed to 92-well tissue culture plates, cultured for 4 wk, and transferred to 24 other well tissue culture plates for 2 more wk of culturing. Culture supernatants were harvested and screened for the presence of antibody against autologous tumor tissue. In the case of rectal cancer, supernatants from 6/24 well positively stained the autologous tissue. The reaction products were located at the luminal surface of tumor cells, and the distribution was quite similar to that of carcinoembryonic antigen. In the case of gastric cancer, supernatants from 7/24 wells positively stained the autologous tissue. The results demonstrate that human antibodies against human tumors and normal tissues can be produced by EBV transformation of lymphocytes, suggesting that there is potential clinical application of this technique for treating tumors and that lymphocytes producing autoantibodies against normal tissues could be easily cultured from the lymph nodes adjacent to tumors. (6 Refs)

2. CHARACTERIZATION OF A MONOCLONAL ANTIBODY TO L1210 LEUKAEMIA.

Testorelli C, Morelli S, Goldin A, Nicolin A
NCI, NIH, Bethesda, MD, 20205
Br J Cancer; 45(3):395-402 1982

A mouse monoclonal cell line (L1) was produced by fusing the mouse myeloma P3X63/Ag8 with CD2F1 spleen cells immunized with a highly immunogenic subline of L1210 leukemia (L1210/DTIC). A very few positive clones (1%) were isolated and one of these was chosen for detailed study. The monoclonal antibody L1 is an IgM immunoglobulin strongly reacting in a complement-dependent cytotoxicity assay against L1210/Cr leukemia and its more or less immunogenic sublines. The specificity of the L1 antibody against L1210 leukemia was studied by extensive screening with normal adult and fetal tissues, lymphoid tissues from several independent strains and a panel of the most common experimental tumors, to all of which it was unreactive. Attempts at immunotherapy were carried out in DBA/2 mice challenged with L1210 leukemia and treated with L1 (ascites) and complement. Although the in vitro cytotoxic titer of ascites fluid from mice bearing hybridoma was very high (10(-7)), no therapeutic effect was obtained in vivo. (Author abstract) (29 Refs)

3. ANALYSIS OF IMMUNOSUPPRESSOR CELLS INDUCED BY IMMUNIZATION OF SOLUBILIZED TUMOR-ASSOCIATED ANTIGENS PREPARED FROM A RAT FIBROSARCOMA.

Minami A
Dept. Orthopedic Surgery, Sch. Medicine, Hokkaido Univ., Sapporo, Hokkaido, Japan
Nippon Seikeigeka Gakkai Zasshi; 55(8):779-792 1981

Soluble tumor antigens were prepared from chemically-induced rat fibrosarcoma KMT-17 cells by sodium deoxycholate (DOC) extraction. Significant responses detected by the footpad assay and Winn assay were demonstrated in rats immunized with DOC extract. However, rats previously immunized with DOC extract showed a significant enhancement of tumor growth when challenged with KMT-17 cells. This enhancement was specific for the tumor line used. The tumor-neutralizing ability of KMT-17 immune spleen cells was abrogated when DOC extract immune spleen cells were added to a mixture of KMT-17 cells and KMT-17 immune spleen cells. This suppressive activity of the spleen cells was diminished by the treatment with anti T serum and complement. After fractionation of DOC extract immune spleen cells by the Ficoll density gradient, the cells in the light layer showed an enhancing effect on tumor growth, whereas the cells in the heavier region of the gradient had an inhibiting effect. These results suggested that both immunosuppressor cells and cytotoxic cells were induced in rats immunized with DOC extract. (Author abstract) (29 Refs)

4. HUMAN MYELOMA CELL LINE CARRYING A PHILADELPHIA CHROMOSOME.

Karpas A, Fischer P, Swirsky D
Dept. Hematological Medicine, Cambridge Univ. Clinical Sch., Cambridge CB2 2QL, England
Science; 216(4549):997-999 1982

A new human plasmacytoma cell line (Karpas 707) has been established from a myeloma patient. The culture cells are negative for Epstein-Barr viral nuclear antigen and free of mycoplasma. They are similar to plasma cells and secrete only lambda light chains. The cells are hypodiploid and contain the Philadelphia chromosome and other abnormalities. This cell line must be suitable for the production of human monoclonal antibodies. (Author abstract) (16 Refs)

TUMOR ANTIBODIES ASSOCIATED WITH VIRUSES

5. ASYMPTOMATIC TYPE C VIRUS CARRIERS IN THE FAMILY OF AN ADULT T CELL LEUKEMIA PATIENT.

Miyoshi I, Taguchi H, Fujishita M, Niiya K, Kitagawa T, Ohtsuki Y, Akagi T
Dept. Medicine, Kochi Medical Sch., Oko-cho, Nankoku-shi, Kochi-ken 781-51, Japan
Gan; 73(2):339-340 1982

Serologic and virologic studies were performed in 14 members of the family of a 49-yr-old male patient with adult T cell leukemia (ATL). The patient and family lived in Kochi, an area where the incidence of ATL appears to be relatively high. ATL antigens (ATLA) and Type C virus particles were detected in short-term cultures of peripheral lymphocytes from 4/5 family members who were ATLA antibody positive. The five ATLA antibody positive family members were all asymptomatic and hematologically normal except for one member, in whom a persistent leukocytosis with several percent abnormal lymphocytes had been observed for two yr. It was not yet determined whether vertical or horizontal infection was involved in the virus transmission in this family. (5 Refs)

6. LOSS OF IMMUNOCOMPETENCY IN HOMOSEXUALS: A NEW PROBLEM.

Hawkins JN, Smith JG
Dept. Dermatology, Medical Coll. Georgia, Augusta, GA, 30912
South Med J; 75(5):516-518 1982

Loss of immunocompetency and increased frequency of Kaposi's sarcoma (KS) in homosexuals is discussed. High serum antibody titers to cytomegalovirus (CMV) were present in all KS patients in whom it was tested. Homosexuals have long been known to have an increased incidence of many infections including hepatitis A and B, amebiasis, giardiasis, gonorrhea, syphilis, condylomata acuminata, and CMV. CMV is believed to be sexually transmitted, and this virus has been demonstrated in both urine and semen. CMV has been shown to cause immunosuppression in mice and human beings. Whether CMV is oncogenic is not known. (12 Refs)

7. REACTIVATION OF EPSTEIN-BARR VIRUS IN PREGNANT WOMEN: SOCIAL FACTORS, AND IMMUNE COMPETENCE AS DETERMINANTS OF LYMPHOPROLIFERATIVE DISEASES - A HYPOTHESIS.

Purtilo DT, Sakamoto K
Dept. Pathology, Univ. Nebraska Medical Center, 42nd and Dewey Ave., Omaha, NE, 68105
Med Hypotheses; 8(4):401-408 1982

Epstein-Barr virus (EBV) appears to be reactivated in women during pregnancy, with resulting formation of anti-EBV antibodies. The stage in life at which an individual is infected by EBV appears to have an effect on the results of infection. Early infection, as might occur when a young child is exposed to his pregnant mother, may result in silent seroconversion. If exposure does not happen until later in life the result may be infectious mononucleosis. Thus, the time of infection may be related to the number of children in a family which sometimes is related to social class. (29 Refs)

8. MONOCLONAL ANTIBODIES FROM MICE BEARING POLYOMA VIRUS-INDUCED TUMOR.

Moav N, Smorodinsky NI, Balin BA, Witz IP
(c/o Smorodinsky) Dept. Microbiology, G. S. Wise Faculty Life Sciences, Tel Aviv Univ., Tel Aviv 69978, Israel
Cancer Immunol Immunother; 12(3):217-224 1982

Antibodies directed against antigens expressed on SEYF-a cells, a polyoma virus-induced sarcoma propagated in syngeneic A.BY mice, were studied and the binding characteristics of some of the resulting autologous monoclonal antibodies to various tumor cell lines and other properties of these antibodies are described. Spleen cells from SEYF-a-bearing mice 4-6 wk after transplantation were used for the hybridization experiments; 45 hybridomas were found to be positive. The antibodies produced by hybridoma F4/5.10 demonstrated high binding activity only to SEYF-a cells and very low binding to KREBS and ELD cells. Results suggested that F4/5.10 produces antibody directed against an antigenic determinant present predominantly on the SEYF-a cell membrane. Three of hybrid clones were found to produce IgG2a, three produced IgG1, and one produced IgM. The heavy chains of F4/5.10 and P3 were in the gamma-chain region, whereas the heavy chains of F7/129.7 were in the mu-chain region. When antibodies from F4/5.10 were used only SEYF-a cells (and none of the other tumor cells tested) absorbed considerable amounts of the antibodies (65%). These results, together with the results obtained from the binding experiments, strongly support the assumption that F7/129.7 antibodies are directed against a broadly distributed public determinant, while F4/5.10 antibodies are directed against a specificity that has a narrow distribution. (33 Refs)

9. VACCINATION AGAINST CHICKENPOX IN CHILDREN WITH LEUKEMIA.

Just M
Universitats-Kinderklinik, Ch-4058 Basel, Switzerland
Monatsschr Kinderheilkd; 129(2):71-72 1981

Eight children with leukemia were vaccinated against chickenpox. Four children showed good induction of antibodies against varicella. Two children produced only small amounts of antibodies; one of these, however, did not develop an infection when exposed to chickenpox. Two children showed development of antibodies only after a second vaccination. Serological examination of one child 6 mo after vaccination showed no remaining antibody; the child did not develop chickenpox after exposure. In current practice children with leukemia are tested for varicella antibodies when possible at diagnosis, before cytostatic therapy. If antibodies are found, no further vaccination is given. If no antibodies are found, zoster immunoglobulin is given during the induction phase of leukemia therapy. If the patient is in remission, and cytostatic therapy can be interrupted for 2 wk, varicella vaccination is administered 1 wk after the last cytostatic treatment. If no antibodies are detected 2-4 wk after vaccination, zoster immunoglobulin therapy must be continued or vaccination repeated. No side effects have been noted with cutaneous or sc vaccination. Vaccination induces production of humoral antibodies and specific cellular immune reactions. Vaccination protects healthy and leukemic children from infection after exposure to chickenpox. (no Refs) (In GER)

ANTITUMOR ACTIVITY AND IMMUNOTHERAPY

10. A MONOCLONAL ANTIBODY (B72.3) DEFINES PATTERNS OF DISTRIBUTION OF A NOVEL TUMOR-ASSOCIATED ANTIGEN IN HUMAN MAMMARY CARCINOMA CELL POPULATIONS.

Nuti M, Teramoto YA, Mariani-Costantini R, Hand PH, Colcher D, Schlom J

Lab. Cellular and Molecular Biology, NCI, NIH, Bethesda, MD, 20205

Int J Cancer; 29(5):539-545 1982

We report here both the range and patterns of reactivity of an IgG1 monoclonal antibody, B72.3, prepared against human metastatic mammary carcinoma cells. When the avidin-biotin complex (ABC) immunoperoxidase technique was used on tissue sections, monoclonal B72.3 reacted with 19 of 41 (46%) primary mammary carcinomas and 13 of 21 (62%) metastatic lesions, either in axillary lymph nodes or at distal sites. Variable concentrations of antigen, recognized by B72.3, were observed among mammary tumors, as well as among different cell populations of a given tumor mass. Several patterns of antigen distribution were observed: membrane, diffuse cytoplasmic, focal, apical and marginal. No reactivity was observed to normal mammary epithelium, stroma, or lymphocytes of the breast, nor to any cell types in a variety of other normal human tissues, melanomas, and sarcomas. Reactivity with all of four colon carcinomas was also observed. Assay of serial sections of mammary carcinomas with B72.3 and a monoclonal antibody directed against carcinoembryonic antigen demonstrated that these antigens were both distinct and non-coordinately expressed. (Author abstract) (17 Refs)

11. THE MEASUREMENT OF LEUKOCYTE SUBSETS IN THE PERIPHERAL BLOOD OF CANCER PATIENTS WITH SOLID TUMORS USING MONOCLONAL ANTIBODY REAGENTS.

Harris JE, DeBoer KP, Vahey AL, Braun DP
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Med Pediatr Oncol; 10(2):185-194 1982

Monocyte and lymphocyte subsets were quantitated in the peripheral blood of normal subjects and patients with solid tumors using the monoclonal antibody reagents OKM1, BRL63D3, OKT3, OKT4, and OKT8. Percentages and numbers of cells reacting with monoclonal reagents were analyzed by indirect immunofluorescence. Correlations between leukocyte subset values and stage of disease or immunocompetence were sought. No differences from normal were seen in the percentage of OKT3, OKT4, and OKT8 cells or in the ratios of OKT4/OKT8 cells in peripheral blood mononuclear cells (PBMC) from all cancer patients, patients with localized disease, or patients with advanced disease. A significant decrease in absolute numbers of lymphocytes, OKT3 cells, OKT4 cells, and OKT8 cells was seen in the peripheral blood of patients with advanced disease reflecting the absolute lymphopenia of these patients. A significant increase was seen in the percentages of PBMC reacting with OKM1 and BRL63D3 from patients with advanced disease compared with normal donors of localized disease patients. A positive correlation was found between PHA responsiveness and absolute numbers of OKT3 and OKT4 cells. A negative correlation was found between PHA responsiveness and percentages of OKM1 cells. These data indicate that malignant disease does not alter T cell subset percentages in patient peripheral blood but may decrease their absolute numbers in association with absolute lymphopenia. On the other hand, percentages of OKM1 and BRL63D3 cells are increased in patients with advanced solid tumors in association with impaired PHA responsiveness. (Author abstract) (19 Refs)

12. MONOCLONAL ANTIBODIES AGAINST A SOLUBLE CYTOPLASMIC ANTIGEN IN HUMAN PROSTATIC EPITHELIAL CELLS.

Clarke SM, Merchant DJ, Starling JJ
(c/o Merchant) Dept. Microbiology and Immunology, Eastern Virginia Medical Sch., Norfolk, VA, 23501

Prostate; 3(2):203-214 1982

Spleen cells from Balb/c mice immunized with a soluble cytoplasmic protein extract from benign prostatic hyperplastic tissue were fused with P3 X63 AG8 myeloma cells. Monoclonal antibodies from the resulting hybridoma were used in either an indirect immunofluorescence or a biotin/avidin immunoperoxidase technique to stain frozen sections of prostate tissue, primary epithelial outgrowth from prostate explants, and cultured prostatic epithelial cells. The antibodies recognized prostate epithelial cells which surround the acini, but did not stain the fibromuscular stroma. The antigen detected, which is distinct from prostatic acid phosphatase, is believed to be a product of differentiated prostate acinar cells, and may be useful marker for studying prostatic cancer cells in culture. (11 Refs)

13. AN IMMUNOHISTOCHEMICAL STUDY OF NASOPHARYNGEAL NEOPLASMS USING KERATIN ANTIBODIES. EPITHELIAL VERSUS NONEPITHELIAL NEOPLASMS.

Madri JA, Barwick KW
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Am J Surg Pathol; 6(2):143-149 1982

Keratin antibodies (KA) were used for differential diagnosis of epithelial neoplasms from nonepithelial neoplasms in 40 patients with nasopharyngeal neoplasms. KA titered out to a dilution of 1:3,200 using an initial dilution of 1:100. The antigen-antibody reaction was completely inhibited by the addition of microgram quantities of keratin prior to incubation on antigen-coated plates. Positive, specific labeling was observed in unfixed frozen sections without the use of pronase treatment, while formalin-fixed, paraffin-embedded tissue sections required pronase treatment for labeling. Twenty-five lesions were classified as squamous cell carcinoma (SCC), 11 were keratinizing, and 15 nonkeratinizing tumors. The subcatergorization is summarized. Seven patients with malignant lymphoma all had positive nasopharyngeal biopsies, but all had additional lymph nodal tissue obtained at subsequent biopsy or autopsy which confirmed diagnosis. Two patients with malignant melanoma (MM) each had a nasopharyngeal tumor characteristic of melanoma, and each had a documented previous cutaneous MM prior to the nasopharyngeal lesion. With immunoperoxidase staining all SCC were positive for keratin. Nonkeratinizing tumors tended to stain less intently and more focally than keratinizing lesions. Antikeratin staining was in general more intense in well-differentiated tumors as opposed to less differentiated tumors. In poorly differentiated lesions, staining was frequently focal and many cells did not stain. The epithelial cells of the lymphoepitheliomas showed definite staining, but at times this was delicate and not all epithelial clusters stained. One of the undifferentiated malignant neoplasms had a somewhat epithelioid appearance and had originally been interpreted as anaplastic SCC. This technique appears to be a useful, reliable, and sensitive method for diagnosing and classifying nasopharyngeal lesions. (16 Refs)

14. CHARACTERIZATION OF THE ANTIBODIES IN NORMAL RABBIT SERUM RESPONSIBLE FOR THE LYSIS OF NK-SENSITIVE TARGET CELLS.

Urdal DL, Henney CS
Basic Immunology Program, Fred Hutchinson Cancer Res. Center, 1124 Columbia St., Seattle, WA, 98104

Mol Immunol; 19(4):599-608 1982

Normal rabbit serum has previously been reported to lyse a spectrum of murine lymphoid cell lines characterized by being susceptible to natural killer (NK) cells. Although we have failed to confirm that a simple correlation exists between the susceptibility of target cells to NK cells and to normal rabbit serum, we were able to characterize a number of naturally occurring anti-carbohydrate antibodies which selectively lyse NK-susceptible lymphoma cells. The antibodies present in normal rabbit serum responsible for lysing an NK susceptible clone derived from the DBA/2 lymphoma L5178Y (27v-IC2) were found to be directed against the terminal beta-N-acetylgalactosamine sugar present on the neutral glycolipid gangliotriosylceramide. Interestingly, normal rabbit serum did not lyse an NK-insusceptible variant, derived from the same lymphoma, which lacked gangliotriosylceramide. YAC-1 target cells, the prototype target for murine NK cells, were insusceptible to normal rabbit serum. However, following neuraminidase treatment, such cells were lysed by an antibody in normal serum directed against terminal beta-galactose residues. The anti-beta-galactose reactivity was directed against the carbohydrate structure of gangliotetraosylceramide. These findings are discussed in light of the hypothesis that NK cells interact with susceptible target cells through cell surface glycoconjugates. (Author abstract) (23 Refs)

15. THYMOCYTOTOXIC ANTIBODIES IN PATIENTS WITH AUTOIMMUNE HEMOLYTIC ANEMIA, SYSTEMIC LUPUS ERYTHEMATOSUS AND LYMPHOPROLIFERATIVE DISEASES.

Fegiolo E
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Blut; 44(4):225-230 1982

Cytotoxic antibodies against thymocytes and peripheral blood lymphocytes were studied in patients with autoimmune hemolytic anemia (AIHA), active systemic lupus erythematosus (SLE), and lymphoproliferative diseases (LD). Sera of 66 patients were investigated: 25 with idiopathic and 8 with LD-associated AIHA, 23 with LD, and 10 with active SLE. The results of the cytotoxicity tests against thymocytes and T lymphocytes are summarized. The incidence of thymocyte antibodies (TA) was almost twice that of lymphocyte antibodies. No significant difference in the frequency of TA and T lymphocyte antibodies was observed in the single types of LD or between the patients with 'warm' or 'cold' AIHA. Only 42% of the sera containing TA were also reactive against T lymphocytes, whereas 70% of the sera cytotoxic for T lymphocytes were also thymotoxic. Thirty-six percent of sera were reactive against both thymocytes and T lymphocytes. Each serum contained antibodies directed against a different number of T lymphocyte samples without it being possible to statistically show specificities with particular HLA-A or B antigens. The percentage of cytotoxicity varied among the sera from patients with the same disease. The extent of thymocytotoxicity was always different from that of T lymphocytotoxicity for sera showing both reactivities. In both cytotoxicity tests for T lymphocytes and thymocytes, the percentage of variation of dead cell counts between duplicate assays was 5% or less. The distribution of dead cells in the thymocytotoxicity test in different diseases is presented. (25 Refs)

16. MECHANISMS OF IMMUNITY IN CANCER.

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Cancer Res. Campaign Lab., Univ. Nottingham, Nottingham NG7 2RD, England
Pathobiol Annu; 11:155-175 1981

Immunological recognition of malignant cells in human tumors, malignant melanomas, and other tumors, and the role of suppressor T cells and other suppressor factors are discussed. The tumor cell must express an appropriate tumor associated antigen for a tumor to generate specific T lymphocyte response and/or initiate antibody formation. Original evidence cited in identifying human tumor associated antigens showed that peripheral blood lymphocytes from patients were cytotoxic in vitro when tested on cultured tumor cells, reactivities indicating that many tumors exhibited tumor-type specific antigens. The reactivity of monoclonal antibody (MCAB) produced by two hybridoma lines prepared against human osteogenic sarcoma cell line is presented. Production of MCAB to melanoma associated antigens by hybridomas derived from fusion of mouse myeloma cells and spleen cells from mice immunized with cultured melanoma cells or membrane fractions was observed. The antibody preparation reacted strongly with cells of the immunizing melanoma and less strongly with an allogeneic melanoma. MCAB specifying cell surface antigens have been produced against other human tumors, including carcinomas of the colon, neuroblastoma, and leukemic cells. MCAB are being produced against a number of tumor associated substances, including carcinoembryonic antigen, human alpha-fetoprotein, and human fibrinolectin. Virus related antigens upon tumor cells, such as Epstein Barr virus antigens, also can be detected by MCAB reagents. Adoptive transfer experiments also have been used to demonstrate a requirement for specifically sensitized T lymphocytes in tumor rejection. One of the most significant aspects of T lymphocyte recognition of tumor associated antigens is the finding that T suppressor cells rather than T cells mediating tumor rejection may be induced. (102 Refs)

17. INHIBITION OF ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY (ADCC) BY NORMAL AND PATHOLOGICAL SERA FROM PATIENTS WITH ADVANCED LUNG CANCER.

Fekete B, Sachno L, Tamassy K, Pal A, Angyal I, Forral I
Natl. Koranyi Inst. for Tuberculosis and Pulmonology, Piheno ut 1, H-1529 Budapest, Hungary
Haematologia (Budap); 14(4):417-423 1981

Technical variables interfering with the detection of Fc-receptor blocking activity of tumor sera were studied using sera from 37 lung cancer patients and 40 normal donors. Washing of effector cells preincubated with pathological sera did not affect the level of inhibition of antibody-dependent cellular cytotoxicity (ADCC). The ADCC inhibition test proved to be reproducible both with and without preincubation and washing. The inhibition of ADCC by sera was not attributable to a direct cytotoxic effect since no difference in viability of target cells treated with human serum albumin, mixed AB serum, or inhibitory sera was observed by trypan blue exclusion. Inhibitory activities of normal and tumor sera were measured in two lymphocyte donors. Serum concentration affected the degree of inhibition, but an increase in the efficacy of inhibition attributed to an increase in concentration was statistically linear only in certain combinations. The difference between tumor and control sera was statistically highly significant in all the experiments. When analyzing the percentage inhibition of ADCC produced by sera, functions able to discriminate between normal and tumor sera could be established. Data presented showed that discriminatory ability of the functions was optimum at serum concentration of 4% for Donor 2 and at 20% for Donor 1. Results indicated that both normal and tumor sera from patients with advanced lung cancer contain blocking factors which may be responsible for the impairment of ADCC activity, but the levels of inhibition exerted by tumor sera are significantly higher than those of normal sera. (21 Refs)

18. EFFECTS OF ANTIBODIES TO CHORIOGONADOTROPIN IN MALIGNANT GROWTH. I. RAT 3230 AC MAMMARY ADENOCARCINOMA.

Kellen JA, Kolin A, Acevedo HF
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Cancer; 49(11):2300-2304 1982

To determine whether the in vivo production of antibodies against choriogonadotropin (CG) could modify the relationship between host and malignant growth, the effects of preimmunization with a conjugate of the beta-subunit of CG and tetanus toxoid (CGbeta-tt) on the development and growth of lung metastasis following iv injection of R 3230 rat mammary adenocarcinoma cells into Fischer 344 female rats have been investigated. This neoplasm has been previously demonstrated to synthesize CG-like material. A test group of 70 animals and two matched control groups of 15 animals each were used. One of the control groups was untreated and the other received tetanus toxoid only. All the control animals had multiple lung foci of neoplastic cells 10 days after seeding, as has been previously observed, and CG antibodies were undetectable. In contrast, a significant titer of anti-CG was found in all preimmunized animals. At the same time, the pretreated animals rarely had a few small neoplastic nodes in the entire lung sections at the standard 8-10 days post-seeding. The protective effects of preimmunization with CGbeta-tt were further demonstrated by the animals living 20 days post-seeding, the absence of lung pathology in the ones killed thereafter, and by six animals that were left alive and have not shown any deterioration for more than 6 mo after the administration of the cell suspension. (Author abstract) (38 Refs)

19. MEDULLOBLASTOMA AND NEUROBLASTOMA IN ADULTS.

Blijham GH, Barlogie B, Richman S, Latreille J, Vellekoop L
Dept. Internal Medicine, Hosp. 'St. Annadal', P.O. Box 616, 6200 MD Maastricht, The Netherlands
Neth J Med; 25(4):94-99 1982

Radiotherapy, chemotherapy, and prognosis of adult medulloblastoma and neuroblastoma are reviewed. Medulloblastoma in a 24-yr-old white male and neuroblastoma in a 19-yr-old white male are described and discussed. Medulloblastoma is characterized by dissemination of tumor cells via the cerebrospinal fluid from the primary localization in the posterior fossa to the subarachnoid space elsewhere. Neurosurgical treatment is insufficient to control the primary site or to prevent metastatic spread. Radiotherapy alone may be sufficient for cure of adult medulloblastoma, and recurrent cases may be successfully treated by combination chemotherapy, although few studies have been done. Adult neuroblastoma can be distinguished from benign or malignant pheochromocytoma by its malignant potential being much greater, lack of symptoms related to excessive release of catecholamines, and its histologic appearance. The majority of patients with neuroblastoma, whether children or adults, may benefit from chemotherapy. Neuroblastoma has more spontaneous regressions than any other malignant tumor; it may undergo spontaneous or therapy-induced maturation to more benign forms, and some cases of cellular or humoral immunity against tumor cells have been observed. Prolongation of survival in adult medulloblastoma and neuroblastoma by radiotherapy and chemotherapy is a realistic goal. (35 Refs)

20. IMMUNOHISTOCHEMICAL ANALYSIS OF THE DISTRIBUTION OF LYMPHOCYTE SUBPOPULATIONS IN HODGKIN'S DISEASE.

Borowitz MJ, Croker BP, Metzgar RS
Dept. Pathology, Duke Univ. Medical Center, Box 3712, Durham, NC, 27710
Cancer Treat Rep; 66(4):667-674 1982

We studied the histologic distribution of lymphocyte subpopulations in Hodgkin's disease. Involved tissues from 15 patients were stained by an indirect immunoperoxidase procedure for a variety of lymphocyte surface antigens using monoclonal antibodies. In most cases, there were more T cells than B cells, and Reed-Sternberg cells were found in T-cell-rich areas. Except in lymphocyte-depleted Hodgkin's disease, helper-T antigen-positive (TH) cells greatly outnumbered cytotoxic-suppressor antigen-positive cells. Moreover, TH cells showed a preferential association with Reed-Sternberg cells. Lymphocytes surrounding Reed-Sternberg cells often expressed the transferrin receptor, a marker of cell activation. Our results do not support the hypothesis that the lymphocytes in Hodgkin's disease represent a cytotoxic T-cell response to neoplastic cells, except perhaps in the lymphocyte-depleted subtype. (Author abstract) (24 Refs)

21. ABILITY OF TUMOR CELLS TO RESIST HUMORAL VS. CELL-MEDIATED IMMUNE ATTACK IS CONTROLLED BY DIFFERENT MEMBRANE PHYSICAL PROPERTIES.

Schlager SI
Dept. Microbiology, Univ. Notre Dame, Notre Dame, IN, 46556
Biochem Biophys Res Commun; 106(1):58-64 1982

Treatment of P815 murine mastocytoma cells with adriamycin increased their susceptibility to killing by antibody + complement (Ab-C) compared to controls; mitomycin C did not show this effect. Cells washed free of the drug and incubated in the drug-free medium regained control levels of susceptibility to Ab-C. Opposite effects of these two drugs on the susceptibility of P815 cells to killing by cytotoxic T-lymphocytes (CTL) were observed, ie, mitomycin C, but not adriamycin, increased the susceptibility to CTL killing. Cells washed free of drug and reincubated in drug-free medium reverted to control levels of susceptibility to CTL. P815 cells cultured with hydrocortisone were rendered more resistant, compared to controls, to Ab-C or CTL killing; epinephrine treatment had no effect on the susceptibility to either Ab-C or CTL attack. Cells washed free of hormone again reverted to control levels of susceptibility to Ab-C and CTL. Membranes from adriamycin-treated cells exhibited increased membrane fluidity compared to controls; mitomycin C had no effect. Hydrocortisone treatment decreases membrane fluidity while epinephrine had no effect. Mitomycin C decreased, and hydrocortisone increased, the net negative cell surface charge density. Adriamycin and epinephrine had no effect. Drug- or hormone-treated reverted cells were similar to control cells in membrane fluidity and surface charge. These results indicate that plasma membrane fluidity and cell surface charge are unique physical properties that control the susceptibility of tumor cells to Ab-C and CTL killing, respectively. (19 Refs)

22. SUPPRESSOR CELLS AS AN AGENT OF IMMUNE FACILITATION II. ADOPTIVE TRANSFER OF PASSIVELY INDUCED ENHANCEMENT OF ALLOGRAFTED TUMORS.

Douvas GS, Kinsky RG, Duc HT, Voisin GA
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Cell Immunol; 68(2):389-401 1982

CBA mice injected intravenously with CBA anti-A/J spleen cell antiserum, and challenged subcutaneously 24 hr later with A/J-derived sarcoma 1 (sa 1) develop progressive tumors. 'Normal' CBA mice (ie, injected with normal CBA serum or noninjected) reject the allograft within 20 days. Spleen cells taken from mice 20-35 days after the injection of antiserum and Sa 1 challenge can specifically transfer the ability to enhance tumor growth when injected into 200 rad irradiated recipients. Spleen cells taken 8 days after antiserum and Sa 1 challenge cannot transfer suppression. The induction of suppressor cells requires both antiserum treatment and Sa 1 challenge. Serum from suppressed mice, and from control mice that are rejecting their tumors, can also transfer suppression but only when taken 20-35 days after treatment. The suppressor cells function most effectively when transferred at the time of tumor challenge, however, they also inhibit the rejection of Sa 1 when mixed with nylon-wool purified sensitized T cells. Suppressor cells are both nylon-wool nonadherent and adherent. Further purification of the column-enriched cells using antiimmunoglobulin or anti-Thy 1.2, plus complement, suggests that both T and B cells can suppress. The mixed lymphocyte response (MLR) of spleen cells from mice challenged only with Sa 1 is inhibited 8 days after challenge. A secondary response is obtained at 20-27 days. In contrast, the MLR from antiserum and Sa 1-treated mice 8 days after challenge resembles a secondary response. By 20-27 days mice with progressive tumors have only a primary-like response. In the present experimental situation, mitomycin-treated spleen cells from antiserum and Sa 1-treated mice cannot significantly inhibit the MLR of normal cells. (Author abstract) (20 Refs)

23. MONOCLONAL ANTIBODY BA-1 DOES NOT BIND TO HEMATOPOIETIC PRECURSOR CELLS.

Jansen J, Ash RC, Zanjani ED, LeBien TW, Kersey JH
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Blood; 59(5):1029-1035 1982

Monoclonal antibody BA-1 binds to B-lymphocytes, to cells from most cases of non-T acute lymphoblastic leukemia (ALL), and weakly to neutrophils. To determine whether BA-1 also reacts with hematopoietic progenitor cells (HPC), we studied the effect of removal of BA-1+ cells from human bone marrow on the proliferation in vitro of the trilineage precursor cell CFU-GEMM, and of the committed progenitor cells of granulopoiesis (CFU-C) and erythropoiesis (BFU-E/CFU-E). Complement-mediated cytotoxicity using BA-1 at concentrations far beyond those required to lyse BA-1+ bone marrow cells and ALL cells did not result in inhibition of colony formation in any of the assays. A rosette separation method, using ox red blood cells coated with BA-1, resulted in enrichment of HPC in the BA-1-depleted interface, whereas very few HPC were found in the BA-1-enriched pellet. Both methods indicate that BA-1 does not bind to HPC, although binding of the antibody to the lymphohematopoietic stem cell cannot be excluded yet. The high cytotoxic capacity of the IgM antibody BA-1, and the lack of reactivity with HPC, make the antibody particularly suitable for use in autologous bone marrow transplantation for patients with ALL. (Author abstract) (26 Refs)

24. MURINE MONOCLONAL ANTIBODY THERAPY IN TWO PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA.

Dillman RO, Shawler DL, Sobol RE, Collins HA, Beauregard JC, Wormsley SB, Royston I
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Blood; 59(5):1036-1045 1982

We infused the murine monoclonal antibody T101 into two patients with advanced refractory chronic lymphocytic leukemia (CLL) after confirming its reactivity with their CLL cells. One patient received doses of 1, 3, and 12 mg; the second patient received 10 mg. Antibody was delivered over 10-15 min. The major observations were: (1) T101 murine monoclonal antibody did bind to cells with T65 surface antigen and saturated these cells in vivo; (2) cells that bound T101 disappeared from the circulation by 2 hr after treatment, as evidenced by a marked drop in lymphocyte counts; (3) T101 serotherapy resulted in some intravascular cell injury associated with sequestration and probably destruction in the liver and lung; (4) free serum T101 was demonstrable, but disappeared by 2-4 hr after infusion; (5) rapid infusion of T101 did not induce significant modulation of T65; (6) rapid infusion of greater than 10 mg of T101 was associated with significant systemic reactions. Monoclonal antibodies may someday have an application in leukemia therapy, but additional experimental trials are clearly indicated. (Author abstract) (26 Refs)

IMMUNOGLOBULIN STRUCTURE AND SYNTHESIS

25. REGULATION OF CATABOLISM OF IGM HEAVY CHAINS IN A B LYMPHOMA CELL LINE.

Dulis BH, Kloppel TM, Grey HM, Kubo RT
Dept. Medicine, Natl. Jewish Hosp. and Res. Center, Denver, CO, 80206
J Biol Chem; 257(8):4369-4374 1982

The human lymphoma cell line Daudi has the phenotype of a nonsecreting B cell. This cell line synthesizes both the membrane and secreted forms of the IgM heavy chain, but only expresses functional membrane IgM. We have found that secreted type heavy chains (mu s) are rapidly degraded in these cells, with a half-life of 1.3 h. Some of the membrane type heavy chains (mu m) are also rapidly catabolized but some are expressed in a stable form with a half-life of 13 h. Inhibiting the initial glycosylation of heavy chains with tunicamycin has differential effects on the catabolic rates of mu s and mu m chains. The turnover of mu s chains is not affected by this inhibitor, but the degradation of mu m chains is much more rapid after tunicamycin treatment. In comparison with their glycosylated counterparts, nonglycosylated mu chains do not covalently assemble to a significant degree with light chains. Tunicamycin treatment of Daudi cells thus seems to inhibit formation of stable mu m protein, possibly by altering mu chain conformation and inhibiting its interaction with light chains. We conclude from these results that some mu m chains are specifically protected from proteolysis by posttranslational events. These processing events include covalent assembly with light chains, terminal glycosylation, and insertion into the plasma membrane. (Author abstract) (25 Refs)

26. ANTI-IDIOTYPES TO MONOCLONAL ANTI-H-2 ANTIBODIES - I. CONTRIBUTION OF ISOLATED HEAVY AND LIGHT CHAINS TO IDIOTYPE EXPRESSION.

Bluestone JA, Metzger JJ, Knode MC, Ozato K, Sachs DH
Translation Biology Section, Immunology Branch, NCI, NIH, Bethesda, MD, 20205
Mol Immunol; 19(4):515-524 1982

Anti-idiotypic sera were produced by immunization of miniature swine with affinity-purified monoclonal anti-H-2Kk antibodies. The purified anti-idiotypic antibodies obtained by this immunization recognized unique determinants on each monoclonal anti-H-2Kk immunogen and were not broadly cross-reactive with other anti-H-2Kk antibodies. These reagents were used to examine the expression of idiotype on isolated heavy and light chains as well as on reassociated Ig molecules. Minor populations of idiotope(s) could be detected by a direct binding radioimmune assay on isolated heavy chains and on isolated light chains. However, the predominant idiotope(s) were expressed only on native Ig and on isolated heavy chains. The expression of these heavy-chain idiotopes was found to be specifically augmented by the addition of homologous light chains. In contrast, reassociation of heavy chains with light chains from a different anti-H-2Kk monoclonal antibody diminished idiotype expression. A model for the molecular interactions occurring between these molecules is proposed on the basis of these results. The nature of these interactions may also have implications for the analysis of the basis of idiotype expression on anti-MHC T-cell receptors. (Author abstract) (26 Refs)

27. DETECTION AND QUANTITATION OF IMMUNOGLOBULINS ASSOCIATED WITH TUMORS OF THE HUMAN ORAL CAVITY.

Pillai S, Sasidharan VK, Balaram P, Vivekanandan S, Vasudevan DM

Regional Cancer Center, Medical Coll. Campus, Trivandrum 695 011, India

Indian J Cancer; 19(1):44-46 1982

IgA and IgM were quantitated by radial immunodiffusion on agar plates containing IgA, IgG and IgM antisera. Alpha amylase activity was measured in tissue extracts to eliminate saliva contamination which contains high amounts of IgA. IgA and IgG were found only in tumor extracts, supporting the concept of tumor associated antibodies. Potassium chloride was used to extract membrane integral proteins or membrane bound proteins and no IgG was quantitated in these extracts. This suggests that IgG may be present in the cytoplasmic portion of the cell extract or present on the surface of tumor cells attached to other membrane proteins. The role of herpes simplex virus in pathogenesis of oral cancer is discussed; cells transformed by DNA viruses carry virus specific antigens. Immunoglobulins in tumor extracts might also be a reaction to these virus specific antigens. (19 Refs)

28. IDIOTYPE-BEARING LYMPHOID CELLS IN PLASMA CELL NEOPLASIA.

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Clin Haematol; 11(1):65-86 1982

Current evidence for the existence of B lymphocytes as part of the tumor cell clone in multiple myeloma (MM) is discussed and related to tumor cell differentiation and progression. B lymphocytes carrying the light chain isotype of the myeloma protein are selectively increased in the blood of approx half of untreated patients and are also found in the bone marrow when not detected in peripheral blood. Further evidence for the existence in MM of monoclonal B lymphocytes is provided by the varying expression of IgG-Fc- and C3-receptors on idiotypic cells; the presence of idiotypic Ig in some cell cytoplasm; and the morphology of lymphocytes, lymphoplasmacytoid cells, or plasma cells. (60 Refs)

29. GAMMAHEAVY CHAIN DISEASE IN MAN: CDNA SEQUENCE SUPPORTS PARTIAL GENE DELETION MODEL.

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Proc Natl Acad Sci USA; 79(10,part1):3260-3264 1982

Human gamma heavy chain disease (HCD) is characterized by the presence in serum of a short monoclonal Ig gamma chain unattached to light chains. Although most HCD proteins have internal deletions, in some the defect is NH2-terminal. The OMM gamma3 HCD serum protein is of the latter type, having undergone an extensive NH2-terminal deletion with a sequence starting within the hinge. A cell line synthesizing the OMM protein has enabled us to study the biogenesis of the abnormal molecule. In vitro translation of isolated mRNA yields a protein containing a hydrophobic NH2-terminal leader sequence. In the intact cell, the precursor molecule is processed normally to yield a protein with an NH2-terminal sequence homologous to the beginning of the variable (V) region. The nucleotide sequence of cDNA prepared from the OMM mRNA encodes a 19-amino acid leader followed by the first 15 residues of the V region. An extensive internal deletion encompasses the remainder of the V and the entire CH1 domain. Immediately following the short V region, there is information in the cDNA for the entire normal hinge. The primary synthetic product is thus an internally deleted molecule that undergoes postsynthetic degradation to yield the NH2-terminally deleted serum protein. The structure of the OMM mRNA suggests that the protein abnormality results from a partial gene deletion rather than defective splicing. (Author abstract) (45 Refs)

30. HUMAN NEUTROPHIL FCGAMMA RECEPTOR DISTRIBUTION AND STRUCTURE.

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Proc Natl Acad Sci USA; 79(10,part1):3275-3279 1982

Fc receptors (FcR) for IgG on human cells were analyzed with two monoclonal antibodies, 3G8 and 4F7. Fab fragments of both hybridoma IgGs inhibited binding to neutrophils of soluble rabbit IgG complexes and sheep erythrocytes (E) coated with rabbit IgG. The number of sites for 3G8 Fab was 135,000 per neutrophil, roughly equivalent to the number of sites for rabbit IgG in immune complexes (112,000 per cell). We did not observe human IgG1 binding sites on neutrophils, although binding of IgG1 to FcR-bearing lines U937 and HL-60 was readily demonstrated. Other cell types bearing 3G8 binding sites were mature chronic myelogenous leukemia cells, eosinophils, 6% of E-rosetting lymphocytes, and 15% of Ig-bearing peripheral lymphocytes. No binding of 3G8 Fab was observed on the FcR-bearing cell lines U937, HL-60, Raji, Daudi, and K562 or on blood monocytes. However, 15% of monocytes cultured for 7 days and 60% of lung macrophages expressed 3G8 antigen. When analyzed by sodium dodecyl sulfate/polyacrylamide gel electrophoresis, the neutrophil FcR immunoprecipitated with 3G8 or 4F7 Fab-Sepharose displayed a broad band extending from Mr 73,000 to 51,000; in many experiments this band was resolved into two poorly separated components, centered at Mr 66,000 and 53,000. These results show that human neutrophil FcR for IgG is different from that on monocytes, with respect to both antigenic composition and binding of monomeric IgG1. (Author abstract) (35 Refs)

31. POLYMORPHISMS IN IMMUNOGLOBULIN HEAVY CHAINS SUGGESTING GENE CONVERSION.

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Proc Natl Acad Sci USA; 79(10,part1):3280-3284 1982

Complete heavy (H) chain variable region (V region; amino acids 1-118) sequences have been determined for three phosphocholine (PCho)-binding monoclonal antibodies of CBA mouse strain origin. Two of these were found to differ from the sequence of the BALB/c T15 germline VH segment (segment of the V region that includes amino acids 1-95) at four positions but were identical to the allelic form of T15 (C3) found in C57BL. The third VH segment, HP101.6G6 (6G6), was clearly the product of a second, related VH gene, probably the allele of the BALB/c V11 gene, a second member of the P-Cho VH gene family. Thus, more than one VH gene is capable of encoding heavy chains of PCho-binding antibodies. The 6G6 VH segment differs from V11 at seven positions; four of these distinguishing amino acids are encoded in other members of the PCho VH gene family. We postulate that the origin of the 6G6 VH sequence can most easily be explained by a process of gene conversion occurring between at least three members of the PCho VH family. (Author abstract) (43 Refs)

32. LEUKEMIA AS SEEN FROM IMMUNOGLOBULIN: B-LYMPHOCYTE LEUKEMIA AND B-LYMPHOCYTOSIS.

Miyoshi K, Kosaka M, Iguchi K, Umi M, Miyamoto H, Numata S, Shirakami A
First Dept. Internal Medicine, Tokushima Univ. Sch. Medicine, Tokushima, Japan
Nippon Rinsho; 39(8):2806-2814 1981

Normal Japanese shows in general more IgG and IgA, and less IgM and IgD in their surface immunoglobulin (Ig) of peripheral blood lymphocytes, than the Europeans and the Americans. The ratio of kappa to lambda for Japanese is, overall, 1.38, lower than 2.04 for Europeans and Americans. The increase of Ig in B-lymphocytosis induced disorders such as infection, hyperthyroidism, are generally multiclonal in nature. In contrast, in B-lymphocytic leukemia, the increase of Ig is monoclonal in nature. The monoclonal increase of Ig in chronic lymphocyte leukemia, malignant lymphoma, and related leukemia can be seen in marked increase in the amount and in the increased ratio of kappa to lambda. The characteristic of macroglobulinemia is the monoclonal increase of IgM. Recently, (angio)-immunoblastic lymphadenopathy has been drawing attention as a transient type between the reactive type disease and the tumorous disease of B cell because of the multiclonal increase of Ig and a slight monoclonal increase of IgM or IgG. The type of increased B cells in the reactive type diseases or in the malignant diseases can be determined from the type of surface Ig. (29 Refs) (In JPN)

33. IMMUNOGLOBULIN G BIOSYNTHESIS IN A HUMAN LYMPHOBLASTOID CELL LINE. DIFFERENCES BETWEEN MEMBRANE-BOUND AND SECRETORY FORMS OF GAMMA CHAINS.

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Eur J Biochem; 124(1):79-87 1982

The cultured human B lymphoblastoid cell line Maja synthesizes two forms of the gamma heavy chain of immunoglobulin G (IgG) that differ in apparent mol wt. The lower-mol-wt form is secreted into the culture medium as a water-soluble product in association with light chains and comigrates on dodecyl sulfate polyacrylamide gels with serum IgG gamma chains. The higher-molecular-wt form is not detected in culture supernatants. In distinction to the secreted form, the higher-mol-wt form is labeled by a lipophilic, photoactivatable nitrene and is inserted asymmetrically in a transmembrane orientation into rough microsomes. It is concluded that Maja cells synthesize secretory (gammas) and membrane-associated (gammam) forms of IgG heavy chains. Both forms of the gamma heavy chain are glycosylated, and can contain one or two asparagine-linked glycan units. The gammam and gammas heavy chains differ by about 10,000 in apparent mol wt. This difference resides exclusively in the polypeptide moiety. Although part of the difference comprises a transmembrane peptide and a cytoplasmic tail of apparent mol wt about 2,000 for gammam chains, a substantial segment of unique peptide is most probably present on the non-cytoplasmic side of the bilayer. The ionophore monensin inhibits the intracellular transport of gammas and gammam chains at a stage when they are sensitive to the enzyme endo-beta-N-acetylglucosaminidase H. In contrast, HLA-A and HLA-B antigens reach a stage at which they are insensitive to this enzyme in the presence of monensin, although their surface expression is inhibited by the ionophore. The implications of these results for the intracellular transport of membrane-associated glycoproteins are discussed. (Author abstract) (38 Refs)

34. SIMULTANEOUS EXPRESSION OF IMMUNOGLOBULIN MU AND DELTA HEAVY CHAINS BY A CLONED B-CELL LYMPHOMA: A SINGLE COPY OF THE VH GENE IS SHARED BY TWO ADJACENT CH GENES.

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Proc Natl Acad Sci USA; 79(9):2996-3000 1982

The cloned murine B-cell lymphoma line (BCL1) that expresses surface IgM and IgD is considered to be a model for the immunoglobulin gene expression of the mature virgin B cell. Of particular interest is the mechanism by which a single VH gene is shared by two CH genes. We examined the organization of the immunoglobulin heavy chain genes in BCL1 DNA. A single arrangement of CH genes was found with the expressed VHDJH gene complex just 5' to the C mu gene. The complete DNA sequence of the VH gene was determined. No rearrangement occurred in the intervening DNA between the JH and C mu genes or between the C mu and C delta genes. We conclude that dual expression of mu and delta heavy chains using a single VH gene is accomplished by alternate processing of a primary transcript that encompasses the VHDJH complex and both CH genes. (Author abstract) (36 Refs)

35. COMPLETE AMINO ACID SEQUENCE OF THE DELTA HEAVY CHAIN OF HUMAN IMMUNOGLOBULIN D.

Takahashi N, Tetaert D, Debuire B, Lin LC, Putnam FW
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Proc Natl Acad Sci USA; 79(9):2850-2854 1982

We have determined the amino acid sequence of the variable (V) region of the delta heavy (H) chain of human IgD isolated from the plasma of myeloma patient WAH. This V region is usually in its amino end group (arginine) and in its length (129 residues). The length is due to 10 insertions in the third com-

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plementarity-determining region (CDR3). A computer search showed that no reported CDR3-joining region (-JH) sequences are identical and that they appear to be unrelated to the constant (C) region sequences of immunoglobulins. The V region sequence together with our previous results for the C region give the complete sequence of the human delta chain WAH, which has 512 amino acid residues and a Mr approx = 65,000. The human delta chain has four domains (V, Cdelta1, Cdelta2, and Cdelta3) and a long hinge region; by comparison, the mouse delta chain lacks a continuous segment of 135 residues, including half the hinge region and the entire Cdelta2 domain. The human and mouse delta chains also differ in the number, kind, and location of GlcN and GalN glycans and probably in conformation and quaternary structure. These and other considerations suggest that there may be multiple forms of both secreted and membrane-bound IgD that differ in size, structure, and function. (Author abstract) (34 Refs)

36. IMMUNOGLOBULIN HEAVY CHAIN GENE REARRANGEMENT AND TRANSCRIPTION IN MURINE T CELL HYBRIDS AND T LYMPHOMAS.

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Proc Natl Acad Sci USA; 79(9):3015-3019 1982

We have examined the arrangement of immunoglobulin heavy chain constant (CH) and joining (JH) region genes in murine T cell hybrid lines and in T lymphomas. CH genes derived from both parental cell types were present in all hybrids for which polymorphism in sequences flanking CH genes permitted us to distinguish parental CH genes. All T lymphomas and T cell hybrids retained the Calpha gene in germ-line configuration and all but one cell line had germ-line Cmu genes. Novel DNA fragments reactive with JH probes were observed in six of nine T cell hybrids, as well as in two T lymphomas, WEH17.1 and YAC-1, but not in the fusion parent, BW5147. No RNA homologous to Cgamma2b, Calpha, or lambda genes was detected in any of the T cell lines. T cell lines contained poly(A)+ RNA homologous to a Cmu cDNA probe. More importantly, in several cell lines the Cmu RNAs were associated with membrane-bound polyribosomes. These results suggest that both JH rearrangements and Cmu RNA production occur in at least some mature, antigen-specific T cells. They may therefore reflect events in normal T cell development and function related to those involved in the generation of the T receptor for antigen. (Author abstract) (30 Refs)

HUMORAL IMMUNE BLOCKING FACTORS AND ANTIGEN-ANTIBODY COMPLEXES

37. STAGE-ASSOCIATED INCIDENCE OF SERUM CIRCULATING IMMUNE COMPLEXES IN PATIENTS WITH UNTREATED BRONCHOGENIC CARCINOMA.

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Cancer Immunol Immunother; 12(3):197-201 1982

Immune complexes (IC) in serum samples from 46 untreated patients (23 males, 23 females, 37-80 yr old, mean age 60 yr) with bronchogenic carcinoma (BC) were quantitated by means of C1q-binding enzyme-linked immunosorbent assay, and results were compared with those obtained in healthy volunteers. Even though the levels of circulating IC were significantly higher in Stage III than in Stage I BC when analyzed as groups, if only positive patients are considered, the values found in patients between these groups were not statistically different. In 10 patients (5 in Stage I and 5 in Stage III), postoperative serum samples were analyzed for the amount of IC, and no significant differences were found as the result of the tumor removal or debulking within 4-7 days after surgery, nor was a significant difference observed in 5 more patients in whom a later sample at 15 days was studied. A qualitative association between the presence of IC and size of tumor, number of involved lymph nodes, metastasis, grade, cell type, age of patients, survival time, relapses and relapsing time (mean follow-up time was 37 mo, range 24-42 mo), time since onset of disease, and sex was evaluated and found to be negative in all instances. Neither the differences in frequency nor the levels of serum IC were significantly different from those between the granuloma and the nongranuloma patients when analyzed within the nonmalignant control group. Data indicated that the occurrence of IC has neither a prognostic value, as determined after analyzing the late outcome of the patients, nor a diagnostic one, since the incidence of IC in patients with nonmalignant thoracic diseases was found to be similar to that in the BC patients. (20 Refs)

38. C1Q-LATEX ASSAY FOR IMMUNE COMPLEXES.

Medof ME

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J Lab Clin Med; 99(5):678-692 1982

A solid phase radioassay for measurement of ICs in biological fluids is described in which ICs present in test sample bind to C1q immobilized on latex particles and bound complexes are quantitated by reaction with radioiodinated mRF. The radioassay can reproducibly measure 10 ng of aggregated human IgG in serum and differentiate soluble complexes from IC-like materials that precipitate with centrifugation or low temperature or stick to test tube walls. Reagents used in the assay, including C1q-L, can be stored for extended periods of time before use. One hundred four of 171 sera from patients with SLE and 8 of 50 sera from patients with LC, assayed by this method, contained elevated levels of ICs relative to controls. IC levels determined by this method correlated with IC data generated by 125I-C1q-PEG precipitation, Raji cell radioimmune assay, and solid-phase conglutinin assay, in some cases but not others. (Author abstract) (29 Refs)

39. CIRCULATING IMMUNE COMPLEXES (CIC) IN PATIENTS WITH SQUAMOUS CELL CARCINOMA (SCC).

Skeen MJ, Olkowski ZL

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Rev Latinoam Oncol Clin; 13(4):5-8 1981

Circulating immune complexes (CIC) were measured at diagnosis in patients with bronchogenic carcinoma or squamous cell carcinoma of the head and neck. The frequency of patients with elevated CIC was nearly 2x as high in the bronchogenic groups as in the head and neck group. Mean CIC values and CIC range were also higher in the bronchogenic group. Stage IV patients in the head and neck group were more likely to show CIC elevations. In the head and neck group, CIC elevation may be associated with carcinomas with poor prognosis. (9 Refs)

40. GASTRIC CARCINOMA AND THROMBOTIC THROMBOCYTOPENIC PURPURA: ASSOCIATION WITH PLASMA IMMUNE COMPLEX CONCENTRATIONS.

Zimmerman SE, Smith FP, Phillips TM, Coffey RJ, Schein PS
(c/o Schein), Georgetown Univ. Hosp., Room 2230, 3800 Reservoir Road N.W., Washington, DC, 20007
Br Med J; 284(6327):1432-1434 1982

A patient with metastatic adenocarcinoma of the stomach developed microangiopathic hemolytic anemia, thrombocytopenia, renal insufficiency, and fluctuating neurological abnormalities in association with appreciably raised plasma concentrations of immune complexes. This syndrome, similar to thrombotic thrombocytopenic purpura, occurred while the tumor was in sustained objective remission after successful treatment with fluorouracil, doxorubicin, and mitomycin. Reversal of the syndrome was achieved with plasmapheresis, azathioprine, corticosteroids, and antiplatelet treatment; this response was paralleled by a reduction in immune complex concentration, suggesting an immune etiology for the syndrome. Antibodies eluted from the immune complexes reacted with 50% of cells from the gastric cancer but less than 10% of cells from normal gastric mucosa. There was no reactivity with either carcinoembryonic antigen or mitomycin. A 17S immune complex reacted with a glycoprotein from the patient's autologous platelets and produced platelet aggregation. It is postulated that reducing the tumor and the pre-existing state of antigen excess by chemotherapy allowed soluble antigen-antibody complexes to form and the syndrome to develop. (Author abstract) (30 Refs)

HUMORAL IMMUNOSUPPRESSIVE AGENTS

41. THE BIOLOGICAL EFFECTS OF CARRAGEENAN AND OTHER SULFATED POLYSACCHARIDES WITH PARTICULAR ATTENTION TO IMMUNOLOGICAL AND CARCINOGENIC PROPERTIES.

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Ugeskr Laeger; 144(12):860-863 1982

A review of studies on the biological effects of carrageenan shows that induction of colorectal cancer was observed in rats following long-term oral administration of degraded carrageenan. Native (high-molecular-weight) is not known to possess carcinogenic properties. Carrageenan stimulates tumor growth secondarily. The cocarcinogenic effect of carrageenan may be due to its immunosuppressive properties (toxic effect on macrophages and activation of macrophage suppressor cells). (29 Refs) (In DAN)

42. HUMORAL IMMUNOREGULATION IN CANCER PATIENTS.

Urushizaki I, Ishitani K, Ishida N, Herberman RB
Dept. Internal Medicine, Sapporo Medical COll., Sapporo, Japan
Excerpta Med Int Congr Ser; 576:127-146 1981

The effect of serum factors from gastric cancer patients on lymphocyte responsiveness to phytohemagglutinin (PHA) was tested before and after immunochemotherapy with Lentinan (5 mg iv, 2-3x/wk) and Ftorafur (FT-207) (800 mg/day). Cancer sera reduced PHA response of normal lymphocytes, with more suppression with advancing disease. Fractionation of cancer sera by diethylaminoethyl (DEAE) column chromatography yielded nine fractions. Fractions 5 and 6 gave specific PHA response suppression from cancerous sera only. Purification of these showed an acidic alpha-2 macroglobulin component. This component gave significant PHA response suppression at doses greater than 50 ug/ml, and enhanced tumor growth in mice. After immunochemotherapy five responding patients had a reduction of serum immunosuppressive activity, while 10 nonresponders did not. On gel electrophoresis the five responders had a band which might correspond to the LA band of mice, which was not seen in sera from the nonresponders. DEAE fractionation of sera from the responders showed a new band in fraction 4. Purification of this material yielded three peaks, the heaviest of which enhanced PHA responsiveness of normal lymphocytes, and significantly inhibited tumor growth in mice. (13 Refs)

43. IMPAIRED IMMUNOCOMPETENCE IN PATIENTS WITH MALIGNANT GLIOMAS: THE POSSIBLE ROLE OF TG-LYMPHOCYTE SUBPOPULATIONS.

Gerosa MA, Olivi A, Rosenblum ML, Semenzato GP, Pezzutto A, Mahaley MS, Salcman M

Instituto di Neurochirurgia, Universita di Padova, Padua, Italy

Neurosurgery; 10(5):571-573 1982

T suppressor (Tg) and T helper (Tm) cells were analyzed in peripheral blood from 10 patients with malignant astrocytoma and 6 with glioblastoma multiforme (7 men, 9 women; 18-71 yr old) as measures of immunocompetence. Tg and Tm cells were detected using IgG- or IgM-coated ox RBC, respectively. Mean percentage of Tm lymphocytes was considered normal both pre- and postoperatively. However, Tg cells were significantly increased preoperatively as compared to 16 normal controls (18.55 +-1.11 vs 12.72 +-1.19, p less than 0.001), and a slight increase was observed after surgery and radiation therapy. There were no significant differences between the two types of gliomas. The postoperative reduction may be related to chemical- or radiation-induced immunosuppression. The increased numbers of Tg cells found in these patients may correlate with the previously reported impairment of immunocompetence in these brain tumor patients. (17 Refs)

44. IN VITRO AND IN VIVO EFFECTS OF A SUGAR DERIVATIVE OF NITROSOUREA (RFCNU) ON IMMUNE RESPONSE IN THE CANCER PATIENT.

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INSERM Symp; 19:221-228 1981

(Chloro-2-ethyl)-1-(ribofuranosyl-isopropylene-2'-3' paranitrobenzoate-5')-3 nitrosourea (RFCNU) was tested in in vitro studies with lymphocytes and in in vivo studies with patients with either epidermoid lung cancer or digestive tract tumor accompanied by liver or lung metastases. RFCNU is not immunodepressive for the patient as judged by delayed hypersensitivity, auto-rosette levels, and natural killer activity. The drug had low myelotoxicity and was well tolerated even though treatment times were extended due to thrombocytopenia in 30% of the cases. (12 Refs)

45. IMMUNOREGULATORY ACTIVITY OF CELL-FREE PERITONEAL WASHINGS OF MICE WITH EHRLICH ASCITIC CARCINOMA.

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Res Exp Med (Berl); 180(2):147-154 1982

Cell-free peritoneal washings (PW) aspirated from male CBA inbred mice at different time intervals (4, 6, 8, 11, 13, 15, 18, and 19 days) after transplantation of 2.5 x 10(6) Ehrlich ascites tumor cells were subjected to two assays for immunosuppressive activity. Stimulation of human peripheral WBC by phytohemagglutinin was determined by 3H-thymidine incorporation. Inhibition of human WBC migration was determined in the presence of purified protein derivative. PW collected on days 4 and 6 were ineffective, or weakly suppressive, while those collected in advanced and terminal stages of tumor development were suppressive in both tests. Control cell-free PW from normal mice without tumor also exerted suppressive activity when adjusted to the same protein concentration as the PW from mice with Ehrlich carcinoma. This suggests that the host's cells in tumor-bearing animals, rather than tumor cells themselves, may be responsible for the suppressive substance(s). Cell-free PW from mice with advanced tumors stimulated the growth of cultured Ehrlich carcinoma cells, as determined by 3H-thymidine incorporation. (25 Refs)

46. IMMUNOSUPPRESSIVE PROPERTIES OF POLAR ORGANIC COMPOUNDS THAT INDUCE CELLULAR DIFFERENTIATION IN FRIEND ERYTHROLEUKEMIA CELLS.

Suthanthiran M, Rubin AL, Novogrodsky A, Stenzel KH

Rogosin Kidney Center, Dept. Medicine and Biochemistry, Cornell Univ. Medical Coll., New York, NY, 10021

Transplantation; 33(5):534-540 1982

We studied the effect of several polar organic compounds, known to induce erythroid differentiation in Friend leukemia (FL) cells, on in vitro human lymphocyte responses and on skin graft survival in mice. The short chain fatty acids, butyric acid (BA), propionic acid (PA), valeric acid, and the polar organic solvents, dimethyl sulfoxide, dimethylformamide, and dimethylacetamide, all mediated significant inhibition of alloantigen-induced proliferation and generation of cytotoxic T lymphocytes (CTLs) in human primary and secondary mixed lymphocyte culture (MLC) reactions. Hexamethylenebisacetemide, another potent inducer of differentiation in FL cells, also mediated significant suppression. Inhibition of MLC with polar organic compounds was accomplished at concentrations known to induce differentiation in FL cells and that are not cytotoxic to peripheral blood mononuclear cells. In distinct contrast, agents that are structurally related to BA, but that do not induce differentiation in FL cells, such as caproic acid, beta-OHBA, gamma-amino BA, and isobutyric acid, did not exhibit immunosuppressive properties. Pokeweed mitogen-driven polyclonal B cell activation was also suppressed by agents that induce erythroid differentiation in FL cells. In addition to potent in vitro immunosuppressive properties, supplementation of drinking water with BA or PA resulted in prolongation of full-thickness skin grafts in DBA/2 (H-2d) to C57BL/6 (H-2b) donor-recipient combinations. Our findings indicate that polar organic compounds that induce differentiation in FL cells are potent immunosuppressive agents. (Author abstract) (21 Refs)

47. GALLBLADDER CANDIDIASIS IN A LEUKEMIC CHILD.

Schreiber M, Black L, Noah Z, Shulman ST, Yogev R, Venezio FR

(c/o Yogev) Div. Infectious Disease, Children's Memorial Hosp., 2300 Children's Plaza, Chicago, IL, 60614

Am J Dis Child; 136(5):462-463 1982

The case of a 12-yr-old leukemic male in which the primary manifestation of systemic candidiasis was Candida albicans involvement of the gallbladder is presented. Immunosuppression due to administration of adriamycin, cytarabine, carbenicillin disodium, cephalothin sodium, gentamycin sulfate, and trimethoprim - sulfamethoxazole was apparently responsible. Therapy with amphotericin B (1 mg/kg iv every other day) for 6 wk was effective against the candidiasis. (16 Refs)

48. IMMUNOSUPPRESSION IN A HOMOSEXUAL MAN WITH KAPOSI'S SARCOMA.

Rasmussen EO, Cooper KD, Kang K, White CR, Regan DH, Hanifin JM

(c/o Hanifin) Dept. Dermatology, Oregon Health Sciences Univ., 3181 S.W. Sam Jackson Park Road, Portland, OR, 97201

J Am Acad Dermatol; 6(5):870-879 1982

The case of a 34-yr-old homosexual man with Kaposi's sarcoma, as well as cutaneous energy and in vitro evidence of depressed cell-mediated immunity, is described. Cytomegalovirus was isolated from urine and semen. Immunosuppression in this patient and possibly other homosexual men appears to be mediated by abnormalities in the immunoregulatory T lymphocytes. (34 Refs)

OTHER RELATED STUDIES

49. A MONOCLONAL ANTIBODY SPECIFIC FOR A DISTINCT REGION OF HEN EGG-WHITE LYSOZYME.

Kobayashi T, Fujio H, Kondo K, Dohi Y, Hirayama A, Takagaki Y, Kosaki G, Amano T

(c/o Fujio) Dept. Immunology, Res. Inst. Microbial Diseases, Osaka Univ., Yamada-kami, Suita, Osaka 565, Japan

Mol Immunol; 19(4):619-630 1982

Six stable hybrid cell lines that secrete homogeneous anti-hen egg-white lysozyme (HEL) antibodies were prepared by cell fusion between cells of immunoglobulin non-synthetizing myeloma (SP2/0-Ag14) and spleens of A/J mice. One (Hyb - C1) of these hybridoma antibodies was found to be specific for the N- and C-terminal portions of HEL. It showed restricted heterogeneity on isoelectrofocusing and an isoelectric point of about pH 6.0. The heavy- and light-chain classes of the Hyb - C1 antibody were gammal and kappa, respectively. The association constant of the Hyb - C1 antibody with HEL at 37 C was 3.3 x 10(7) (L/M). The Hyb - C1 antibody was further characterized by its cross reactivities with other avian lysozymes. The association constants (KIs) of cross-reactive avian egg-white lysozymes at 37 C, calculated from the inhibitions of binding of 125I-HEL to Hyb - C1 antibody were 3.2 x 10(7) (L/M) for both Japanese quail lysozyme (JEL) and turkey lysozyme (TEL) and 1.2 x 10(6) (L/M) for two duck lysozymes (DL-1 and DL-2). The partial N-terminal amino acid sequences of the heavy and light chains of Hyb - C1 antibody up to the 25th residues were also determined. (Author abstract) (47 Refs)

50. LYMPHOMA IN CARDIAC ALLOTRANSPLANT RECIPIENTS. CLINICAL AND HISTOLOGICAL FEATURES AND IMMUNOLOGICAL PHENOTYPE.

Weintraub J, Warnke RA
(c/o Warnke) Dept. Pathology, Stanford Univ., Stanford, CA, 94305
Transplantation; 33(4):347-351 1982

To characterize further lymphomas which arise in chronically immunosuppressed allotransplant patients, we studied the clinical and histological features of seven cases of nonHodgkin's lymphoma and determined the immunological phenotype in four cases, which developed in a series of 182 patients who underwent cardiac transplantation at Stanford University Hospital. Clinical features which were correlated with the development of lymphoma included patient age, pretransplant diagnosis, and the number of transplants. All cases of non-Hodgkin's lymphoma presented as solitary or multiple localized extranodal lesions while none presented in lymph nodes. Extranodal sites of involvement included brain, lung, and soft tissues of the thigh at the site of antilymphocyte serum injections. Histologically, five of seven lymphomas were classified as high grade, large cell, immunoblastic and two of seven as intermediate grade, large noncleaved cell. The immunological phenotype of the neoplasm from four patients was determined by reaction with immunoglobulin light and heavy chain reagents and monoclonal antibodies to T cell and B cell antigens. All lymphomas from four patients which were tested stained for Ia antigen (HLA-DR) but did not stain for immunoglobulin or the T cell antigens detected in this study. (Author abstract) (33 Refs)

51. EFFECT OF LIPIDS, STRUCTURAL PRECURSORS OF LIPIDS AND FATTY ACIDS ON COMPLEMENT-MEDIATED KILLING OF ANTIBODY-SENSITIZED NUCLEATED CELLS.

Ohanian SH, Schlager SI, Saha S
Lab. Immunobiology, NCI, NIH, Bethesda, MD, 20205
Mol Immunol; 19(4):535-542 1982

The cytotoxic activity of limiting concentrations of human complement against antibody-sensitized line-10 guinea-pig hepatoma cells can be inhibited and/or enhanced by pretreatment of the complement with lipids and/or fatty acids. Cardiolipin (CL), phosphatidylglycerol (PG), phosphatidylcholine (PC), phosphatidylserine (PS), sphingomyelin (SPHMY), cholesterol (CHOL), cholesteryl oleate (CHOL-O), phosphatidic acid (PA) or mammalian phosphatidylethanolamine (PEm) were effective in inhibiting C activity. Bacterial phosphatidylethanolamine (PEb) had no effect. Several cholesteryl esters and triglycerides of known fatty acid composition were tested. CHOL-O and glyceryl-1,2-stearate-3-oleate were effective, but cholesteryl palmitate, stearate, arachidonate and glyceryl-1,3-stearate-2-oleate were not effective in inhibiting HuC action. Structural precursors of phospholipids effective in inhibiting HuC activity (eg, L-alpha-glycerophosphoryl esters of choline, serine and ethanolamine) did not modify the action of HuC on antibody-sensitized line-10 cells under any conditions tested. In contrast to the larger mol wt lipid, conditions were found in which fatty acid could inhibit or enhance the cytotoxic action of C. The modification of C activity was dependent upon the specificity of the antibody used to sensitize the cells, the chain length, and the concentration of the fatty acid. The results suggest that the composition and possible subtle structural characteristics of lipids may play a role in influencing the functional activity of complement. (Author abstract) (33 Refs)

52. IMPROVED HOST DEFENSE AGAINST L1210 LEUKEMIA BY DEPRIVATION OF DIETARY PHENYLALANINE.

Pine MJ
Dept. Experimental Therapeutics, Grace Cancer Drug Center, Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
Nutr Cancer; 3(2):94-102 1981

Restriction of phenylalanine to 0.08%, or less, of the diet has been shown to prolong the survival of L1210 leukemia-bearing DBA/2Ha mice or (DBA/2Ha female x BALB/c male) F1 hybrids. A clonal assay was developed for determining the infiltration of L1210 cells without adaption to cell culture. Phenylalanine restriction significantly reduced the infiltration of ip implanted tumors in tissues of minimal tumor involvement, such as bone marrow and brain. These tumor reductions did not occur with dietary limitations of isoleucine, leucine, cystine-methionine or protein. Tumor infiltration rose to control levels when phenylalanine-limited hosts were immunosuppressed with whole body irradiation or with cyclophosphamide. The L1210-responding BALB/c host when phenylalanine-restricted required a 2-to 3-fold increase in dosage of whole body irradiation in order to succumb to the tumor. In vitro complement-dependent and -independent cytotoxicity of the splenocytes of several host strains immunized to both L1210 cells and sheep erythrocytes were, however, generally reduced by phenylalanine depletion. Phenylalanine depletion is postulated to favor the development of an unidentified immunoproductive and radiation-resistant component of host tumor response. (Author abstract) (9 Refs)

53. IMMUNOGENICITY AND AMPLIFIER CELL PRODUCTION BY TUMOR VACCINES ENHANCED BY CONCANAVALIN A.

Kataoka T, Oh-Hashi F, Sakurai Y
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Gan; 73(2):193-205 1982

The induction of immune resistance to L1210 murine leukemia by three types of L1210 vaccines was compared under conditions in which in vitro cell proliferation and transplantability to mice were completely suppressed. L1210 cells treated with glutaraldehyde plus concanavalin A (ConA) were more potent in inducing antitumor immunity than those treated with Vibrio cholerae neuraminidase or mitomycin C (MMC). This and the finding that cell-bound ConA enhanced the immunogenic potency of MMC- or formaldehyde-treated L1210 vaccine indicate that ConA endowed the cells with additional potency in inducing antibody immunity. ConA-free and ConA-bound vaccine cells took up the same amount of anti-L1210 antibody, suggesting that cell-bound ConA did not increase tumor-associated antigen molecules on the tumor cell surface. However, adoptively transferred spleen cells of mice sensitized with ConA-bound, but not ConA-free, vaccine amplified the vaccine-induced antitumor immunity in the recipients. These donor spleen cells suppressed the in vitro proliferation of live L1210 cells no more than non-primed spleen cells, nor was their amplifying activity abrogated by treatment with anti-Lyt-2.1 antibody and rabbit sera as a source of complement. This indicated that cytotoxic T cells and/or their precursors were not involved in the observed amplification. This as well as the finding that their amplifying activity was completely abrogated by treatment with rabbit anti-mouse brain-associated T cell antigen antisera and rabbit sera as a source of complement, led us to conclude that amplifier T cell production, associated with vaccine-bound ConA, was responsible for the enhanced immunogenic potency of ConA-bound vaccines. (Author abstract) (17 Refs)

54. DOES AN AUTOLOGOUS MIXED LYMPHOCYTE REACTION ACCOUNT FOR THE 'SPONTANEOUS' PROLIFERATIVE ACTIVITY OF PERIPHERAL BLOOD MONONUCLEAR CELLS?

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Cell Immunol; 68(1):173-180 1982

Background and 'spontaneous' proliferation are terms often used for the proliferative activity normally exhibited by peripheral blood mononuclear cells (MNC) in vitro. In this report, we show that Interleukin-2 (IL-2) added to unfractionated MNC but not to isolated T or non-T cells significantly increased their proliferative activity. The cells responding to IL-2 stimulation from MNC were OKT3 positive lymphocytes. In addition, treatment of MNC with either a monoclonal anti-HLA-DR antibody (in the absence of C') or Cyclosporin-A strongly suppressed the 'background' whereas treatment of MNÇ with the 3A1 monoclonal anti-human T cell antibody did not modify 'spontaneous' proliferation of these cells. IL-2 could not restore or increase the proliferative activity of MNC exposed to the anti-HLA-DR antibody or Cyclosporin-A while the T cell growth factor significantly enhanced proliferation of MNC cultured in the presence of the OKT4 antibody. Taken together these results strongly suggest that IL-2 responding T cells from MNC become sensitive to IL-2 by interacting with HLA-DR antigens on B lymphocytes and/or monocytes contained in MNC (resting T cells are Dr-). By a similar mechanism we have previously shown that T cells acquire responsiveness to IL-2 in the autologous mixed lymphocyte reaction (AMLR). Since all the cells that participate in AMLR are present in MNC, we postulate that a 'mini' AMLR taking place within MNC may explain the 'spontaneous' proliferation of peripheral blood mononuclear cells. (Author abstract) (12 Refs)

55. COLIC CARCINOMA AND BASAL CELL EPITHELIOMA ELEVEN YEARS AFTER KAPOSI SARCOMA WITH SPLENIC AND CUTANEOUS INVOLVEMENT.

de Plunkett TL, Pieron R, Dreyfus F, Meyniel D

Service de Medecine Interne, Hopital Tenon, 4, rue de la Chine, 75020 Paris, France

Sem Hop Paris; 58(17):1027-1030 1982

A case of Kaposi sarcoma (KS) with cutaneous and splenic involvement is reported. Carcinoma of the left colon and basal cell epithelioma arose 11 years after KS. Genetic, viral, and immunologic factors which may promote initiation and development of Kaposi sarcoma are reviewed. The responsibility of immunodeficiency, whether resulting from therapy or from other causes, in carcinogenesis is discussed. Prolonged survival may be seen after KS. Another primary malignant disease (lymphoma or solid tumor) may arise. The authors suggest that the risk of immunologic disorders, occurring spontaneously or induced by therapy, should be considered specifically for each patient with KS. (Author abstract) (14 Refs) (In FRE)

56. DETECTION OF RAJI BINDING ACTIVITY IN HYPERIMMUNE ALLOGENEIC TUMOR BEARING SERA ASSOCIATED WITH ANTI-BSA ACTIVITY.

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Res. Inst. Scripps Clinic, La Jolla, CA

Immunol Lett; 4(4):205-209 1982

Brown Norway rats were implanted twice with allogeneic Lewis strain Maloney sarcoma LM-2. The tumor grew progressively for 5 days following implant, followed by a regression phase. During the regression the serum Raji cell binding activity increased, reaching a peak 25 days post-primary implant, thereafter the binding activity decreased. After the second implant, the tumor grew to a peak at 3 days and was eliminated by 10 days. Raji-binding activity increased markedly to a peak at 5 days post-secondary implant and remained elevated up to 40 days. Fractionation of hyperimmune sera in Sephadex G-200 columns revealed that Raji-binding activity was found in fractions co-migrating with rat IgG. Polyacrylamide gel electrophoresis (PAGE) of labeled Raji cell surface components revealed a peak which co-migrated with bovine serum albumin (BSA). This peak was eliminated when radiolabeled surface components were incubated with anti-BSA antiserum before PAGE. Immunodiffusion studies revealed that sera from hyperimmune rats produced a precipitin band with NP-40 lysates of Raji cells and formed a line of identity with BSA. These observations indicate the presence of BSA on the Raji cell surface, and that hyperimmune sera contain anti-BSA IgG antibodies reacting with the cell surface BSA. As a result, in tumor implant models such as this, false positive results can occur due to the presence of anti-BSA antibodies induced and reactive with BSA present on the Raji cell surface. (12 Refs)

57. DIMINISHED HELPER-T-LYMPHOCYTE FUNCTION IN CANCER PATIENTS.

Umeda T, Hara T, Koseki K, Kobayashi K, Akaza H, Niijima T

Dept. Urology, Faculty Medicine, Univ. Tokyo, Bunkyo-ku, Tokyo, Japan

Cell Mol Biol; 28(1):67-71 1982

The induction of immunoglobulin-secreting cells (IgSC) was studied in peripheral blood lymphocytes (PBL) from patients with malignant tumors of the urogenital tract. PBL were cultured in the presence of pokeweed mitogen (PWM) and the number of IgSC was enumerated by reverse plaque technique. It was shown that the generation of IgSC was impaired in lymphocytes from patients with malignancies as compared with those from normal controls. Then, cellular sites responsible for the reduced generation of IgSC in the cancer patients were determined. B-cells from cancer patients generated almost the same number of IgSC as those from normal controls in PWM-stimulated cultures with allogeneic normal T-cells. T-cells from cancer patients showed reduced capacity to induce IgSC in cooperation with allogeneic normal B-cells, as compared with those from normal controls. The generation of Con A-activated suppressor-T cells was not impaired in PBL from cancer patients. Mitomycin-C-treated normal T-cells enhanced the generation of IgSC by allogeneic normal B-cells and the capacity was not impaired in T-cells from cancer patients. From the results obtained, it was suggested that helper-T cells but not suppressor-T-cells nor B-cells were deteriorated in patients with malignancies of the urogenital tract. (Author abstract) (13 Refs)

58. PHENOMENON OF HUMAN T CELLS ROSETTING WITH SHEEP ERYTHROCYTES ANALYZED WITH MONOCLONAL ANTIBODIES: MODULATION OF A PARTIALLY HIDDEN EPITOPE DETERMINING THE CONDITIONS OF INTERACTION BETWEEN T CELLS AND ERYTHROCYTES.

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J Exp Med; 155(5):1317-1333 1982

The monoclonal antibody (MAb) anti-D66, which identifies an epitope that appears to be involved in E-rosette formation, is described. Unlike MAb 9.6, anti-D66 does not block rosettes when erythrocytes have been pretreated with neuraminidase or 2-aminoethylisothiouronium bromide, although it blocks E-rosettes made at both 4 C and 37 C. Cell surface molecules from thymocytes were labeled and isolated by immunoprecipitation and acrylamide gel electrophoresis. D66 and 9.6 epitopes were carried by the same molecule, and although 9.6 epitopes were readily exposed on the cell surface, a large fraction of the D66 epitopes was covered by the glycocalixte, from which it can be unmasked by anti-D66 sensitization plus anti-mouse immunoglobins. D66 is an epitope involved in the interactions between T lymphocytes and erythrocytes, and is clearly different from the epitope defined by MAb 9.6. A striking correlation was observed between the surface density of D66 in a given T cell population and its ability to form stable rosettes at 37 C. (48 Refs)

59. PASSIVE ALLOGRAFT ENHANCEMENT BY SUBCLASSES OF POLYCLONAL ANTIBODIES DIRECTED TOWARD RESTRICTED REGIONS OF THE MAJOR HISTOCOMPATIBILITY COMPLEX.

Duc HT, Kinsky RG, Voisin GA

Centre d'Immuno-Pathologie et d'Immunologie Experimentale de l'INSERM, CNRS (LA 289) Hopital Saint-Antoine, 75012 Paris, France

Transplantation; 33(5):492-499 1982

Two parameters of enhancing major histocompatibility complex (MHC) antibodies, previously separately studied, namely, Ig class and antigen specificity, have been treated simultaneously. In the experimental model used, Sa 1 tumor cells, indigenous of A/J (H-2a) were grafted on CBA (H-2k) or C57BL/Ks (H-2d) mice. Immune sera specific for the H-2 K/D- or H-2 I-coded antigens of the A/J haplotype (anti-Kk, or IAk, IBk, IJk, IEk, or ICd, Sd, Gd, or Dd) and their immunoglobulin fractions (separated on protein A-Sepharose columns) were injected either iv or locally as a mixture with the challenging Sa 1 cells. Within the limits of the studied system, the following results were obtained: (1) Sa 1 cells do possess Iak antigens at their surface detected by C-dependent cytotoxicity; no ICd, Sd, or Gd products were detected. (2) The bulk of enhancing activity is concentrated in IgG1 anti-K/D antibodies (anti-Dd when Sa 1 was grafted on CBA mice and anti-Kk on C57BL/Ks). (3) Anti-Iak antibodies have some activity on Sa 1 cells grafted on C57BL/Ks mice. This activity is significant for IgG1 anti-Iak and suggestive for IgG2 of the same specificity. (4) No enhancing activity was detected in the other antibodies: IgG2 anti-Dd, IgG2 anti-Kk, IgG1, or IgG2 anti-ICd, Sd, Gd as well as in fractions containing IgM and IgA antibodies directed against any studied portion of the MHC products. These results are discussed in terms of the mechanisms involved in enhancement. (Author abstract) (39 Refs)

60. SUBTYPES OF CUTANEOUS T-CELL LYMPHOMA DEFINED BY EXPRESSION OF LEU-1 AND IA.

Wood GS, Deneau DG, Miller RA, Levy R, Hoppe RT, Warnke RA
Dept. Pathology, Stanford Univ. Medical Center, Stanford, CA, 94305
Blood; 59(5):876-882 1982

Monoclonal antibodies were used to characterize immunohistologically the expression of cellular antigens in 25 patients with cutaneous T-cell lymphoma (CTCL). Although all cases expressed the Leu-2a-/Leu-3a+ immunophenotype characteristic of helper T cells, four subtypes were defined based on variable expression of Leu-1 and Ia. In individual patients, the immunophenotype was constant irrespective of body compartment sampled or interim therapy. Ia+ non-T-cells typically constituted one-third of the cellular infiltrate. Along with neoplastic cells, Ia+/T6+ dendritic cells were observed within Pautrier microabscesses, dermis, and individually throughout the epidermis. It will be important to determine if different CTCL immunophenotypes represent different biologic subsets of disease or have prognostic relevance. Prospective studies will be facilitated by single- and double-label immunohistologic techniques that allow the simultaneous evaluation of cellular antigen expression and architectural detail. (Author abstract) (30 Refs)

61. SELECTIVE DEPLETION OF NK CELL ACTIVITY IN VIVO AND ITS EFFECT ON THE GROWTH OF NK-SENSITIVE AND NK-RESISTANT TUMOR CELL VARIANTS.

Kawase I, Urdal DL, Brooks CG, Henney CS
Program Basic Immunology, Fred Hutchinson Cancer Res. Center, 1124 Columbia St., Seattle, WA, 98104
Int J Cancer; 29(5):567-574 1982

Intravenous injection of rabbit anti-asialo-GM serum, an antiserum previously shown to eliminate splenic natural killer in CBA, DBA/2, and BALB/c nu/nu mice. The effect on NK activity was selective. The role of NK cells in controlling tumor cell growth was investigated using an NK-sensitive and an NK-resistant subline of the murine lymphoma L5178Y. The possibility that the effects observed were caused by binding of the injected antibodies to the tumor cells was minimized by: (1) using a clone of tumor cells that lacks chemically detectable asialo-GM, and (2) pretreating animals with anti-asialo-GM rather that administering antiserum and tumor cells concurrently. These studies provided compelling evidence that NK cells could play an active role in controlling tumor growth. Selective depletion of NK activity by injection of anti-asialo-GM serum is a method which would be generally applicable to studying the role of NK cells in disease processes. (28 Refs)

62. REGIONAL LYMPH NODE X-RADIATION SUPPRESSES ALLOGRAFT REJECTION.

Maguire HC, Jaffee BD
Div. Dermatology, Dept. Medicine, Hahnemann Medical Coll., 230 North Broad St., Philadelphia, PA, 19102
Arch Dermatol Res; 272(3/4):283-291 1982

The effect of a single dose of regional lymph node x-radiation (1,000 rads) on allograft rejection was investigated in female mice bearing TA3-Ha A-strain tumors in the rear footpad. Irradiation in C57B1/6 mice resulted in accelerated tumor growth and delayed tumor regression when administered to the hindquarter on the same side as the injected footpad. Irradiation of regional lymph nodes on days 3, 4, or 5 resulted in significantly larger tumors than those in control mice, which received irradiation to the contralateral hindquarter. In DBA/2 mice (which show more aggressive TA3-Ha tumor growth than C57B1/6 mice) tumors often grew progressively and were fatal; progressive tumor growth occurred less frequently in controls that received no irradiation or contralateral irradiation. X-radiation to the field that included regional lymph nodes significantly suppressed tumor rejection in B-cell-deficient C57B1/6 x CBA mice. Cyclophosphamide pretreatment significantly abrogated x-ray-induced immunosuppression. (24 Refs)

63. EBV-IGA AND NEW HETEROPHILE ANTIBODY TESTS IN DIAGNOSIS OF INFECTIOUS MONONUCLEOSIS.

Evans AS, Niederman JC
Dept. Epidemiology and Public Health, Yale Univ. Sch. Medicine, 333 Cedar St., New Haven, CT, 06510
Am J Clin Pathol; 77(5):555-560 1982

An evaluation has been made of the EBV-IgA tests and the immune adherence hemagglutination assay (IAHA) as compared with standard diagnostic procedures in 119 serial sera from 22 clinical and 113 sera from 42 subclinical cases of EBV infectious mononucleosis. EBV-IgA antibody was demonstrable in 86.4% of patients using EB3 cells as antigen and in 68.2% with P3/HRIK cells. For heterophile antibody the IAHA test was more sensitive, gave higher titers, and was positive longer than the standard absorbed horse or sheep RBC tests in both clinical and subclinical EBV infections. (Author abstract) (16 Refs)

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Antibodies and Humoral Immunity

SERIES CB08 No. 82/11

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TUMOR ANTIBODY PRODUCTION/ CHARACTERIZATION/ DETECTION

1. ESTABLISHMENT OF A HUMAN TUMOR CELL LINE FROM A PATIENT WITH PRIMARY HEPATOCELLULAR CARCINOMA (MEETING ABSTRACT).

He L, Wands JR, Quaroni A, Isselbacher KJ
Gastrointestinal Unit, Massachusetts General Hospital, Boston, MA, 02114

Gastroenterology; 83(5,part2):1080 1982

A tumor cell line designated CUSPF (China-United States Peoples Friendship) was established in long-term culture from a hepatitis B surface antigen (HBsAg) negative individual with a poorly differentiated primary hepatocellular carcinoma. The cultured cells have an epithelioid appearance by light and phase contrast microscopy. Scanning electron microscopy revealed extensive microvilli formation on the cell surface as well as communications between cells. Transmission electron microscopy demonstrated a polygonal morphology, with 'epithelioid like' junctions between cells, numerous mitochondria and smooth endoplasmic reticulum, but a poorly developed rough endoplasmic reticulum. Growth curves repeated

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three months apart were identical and demonstrate a doubling time of 48 hours. The CUSPF cells show loss of contact inhibition under confluent conditions. Human chromosomes were identified by isoenzyme analysis. The cells were shown to have aspartate aminotransferase (SGOT) activity but do not synthesize or secrete HBsAg or alpha fetoprotein. Monoclonal antibodies have been prepared to this cell line. The malignant potential of the CUSPF cell line was established by gross tumor formation when injected subcutaneously (1.4x10(7)) into nude mice. The morphology of the solid tumor closely resembles the original hepatocellular carcinoma. Finally, the properties of recultured cells derived from the solid tumor mass grown in nude mice appear to be identical to the original CUSPF cell line. Thus, we have established in culture a human hepatocellular carcinoma cell line. Such cells will be of use in characterization of the malignant properties of human hepatocytes. (no Refs)

2. A MONOCLONAL ANTIBODY RECOGNIZING A HUMAN THYMUS LEUKEMIA-LIKE ANTIGEN ASSOCIATED WITH B2 MICROGLOBULIN (MEETING ABSTRACT).

Knowles RW, Bodmer WF
Imperial Cancer Research Fund, London, England
Eighth Annual Meeting of the American Association for Clinical Histocompatibility Testing, April 25-29, 1982, San Francisco, California. American Association for Clinical Histocompatibility Testing 41 pp., 1982.

A monoclonal antibody, M241, was produced which binds to a human cell surface molecule with properties similar to the murine thymus leukemia (TL) antigen. This human TL-like antigen was found on thymocytes and some T cell lines derived from patients with acute lymphocytic leukemia, but was not found on peripheral blood lymphocytes or B cell lines. The monoclonal antibody M241 was used to immunoprecipitate a molecule from lysates of 125I surface labeled MOLT 4 cells which had two subunits, a 43,000 molecular weight chain and a 12,000 molecular weight chain. The small subunit was shown to be Beta2-microglobulin (beta2-m) by immunoprecipitation with a monoclonal antibody, BBM.1, which recognizes human beta2-m. The TL-like molecule recognized by M241 was shown to be serologically distinct from the HLA-A,B,C molecules recognized by three antibodies W6/32, PA2.6 and BB7.8, and distinct from another human thymocyte antigen, the 49,000 molecular weight HTA 1 molecule, recognized by the monoclonal antibody NA1/34. Following removal of thr HLA-A,B,C molecules, the HTA 1 molecules, and the M241 defined TL-like molecules from MOLT 4 lysates, additional beta2-m associated molecules were immunoprecipitated with BBM.1. These molecules contained a 45,000 molecular weight subunit attached to beta2-m. (no Refs)

3. LARGE-BOWEL CARCINOMAS WITH DIFFERENT PLOIDY, RELATED TO SECRETORY COMPONENT, IGA, AND CEA IN EPITHELIUM AND PLASMA.

Rognum TO, Thorud E, Elgjo K, Bandtzaeg P, Orjasaeter H, Nygaard K
Histochemical Lab., Inst. Pathology, Natl. Hosp., Rikshospitalet, Oslo, Norway
Br J Cancer; 45(6):921-934 1982

Immunofluorescence staining for carcinoembryonic antigen (CEA), secretory component (SC), and epithelial IgA was evaluated semiquantitatively in 85 large-bowel carcinomas in relation to degree of tumor differentiation, Dukes' stage, and plasma CEA level. The tumors were divided into a near-diploid (ND, 28) and an aneuploid group (AN, 57) by means of flow-cytometric DNA measurements. Expression of SC and IgA in neoplastic epithelium was positively related to differentiation in both groups. The AN tumors scored significantly higher for CEA than the ND ones, but the staining was apparently unrelated to differentiation or Dukes' stage. CEA expression in the transitional mucosa adjacent to ND tumors was negatively correlated with tumor differentiation, whereas epithelial IgA and SC in this zone showed a substantially higher positive correlation with tumor differentiation, and a somewhat stronger negative correlation with Dukes' stage in the ND than in the AN group. Plasma CEA levels were significantly related to Dukes' stage, only in patients with AN tumors, and only in this group were positively correlated with estimates of total tumor CEA for Dukes' Stages A and B. For Dukes' Stages C and D (disseminated tumors), moreover, the plasma CEA levels were found to be significantly higher in the AN group. These findings indicate that the DNA profile of large-bowel carcinomas is related both to the way neoplastic cells influence the activity of the transitional mucosa and their capacity for expression and release of epithelial products. AN tumors thus seem to be more active as 'secretors' of CEA than ND ones. (Author abstract) (51 Refs)

4. MONOCLONAL ANTIBODIES TO HUMAN PROSTATE AND BLADDER TUMOR-ASSOCIATED ANTIGENS.

Starling JJ, Sieg SM, Beckett ML, Schellhammer PF, Ladaga LE, Wright GL

Dept. Biochemistry, Eastern Virginia Medical Sch., Norfolk, VA, 23501

Cancer Res; 42(8):3084-3089 1982

Monoclonal antibodies to human prostate adenocarcinoma membrane antigens were produced by fusion of P3X63/Ag8 mouse myeloma cells with spleen cells from BALB/c mice immunized against the prostate cancer cell line DU145. The hybrids were screened for antibody production using glutaraldehyde-fixed cells in a solid-phase radioimmunoassay. Antibody-binding specificity was also checked by quantitative adsorption, membrane immunofluorescence, and complement-dependent cytotoxicity assays. A hybridoma clone (83.21) was isolated that secreted antibodies which preferentially bound to several prostate and bladder cancer cell lines but did not bind to a variety of other normal and malignant human cell lines. This antibody also reacted with a cytomegalovirus-transformed human embryonic lung cell line but not to normal human embryonic lung cells. Quantitative adsorption studies demonstrated that the 83.21 monoclonal antibody was strongly reactive to membrane preparations from human prostate adenocarcinoma tissue and a liver metastasis of prostate carcinoma. Little or no binding activity was observed against two other prostate carcinomas, benign prostatic hyperplasia, normal prostate, or normal liver. Binding studies indicate that the 83.21 monoclonal antibody does not bind to alpha-fetoprotein, carcinoembryonic antigen, prostatic acid phosphatase, human leukocyte antigen, Beta2-microglobulin, HLA-Dr antigens, fibronectin, or prostate antigen. The data indicate that we have isolated a monoclonal antibody that binds to an antigen(s) expressed by several urogenital carcinoma cell lines as well as human prostate tumor tissue and that the antibody is not directed against well-known human tumor cell markers. (Author abstract) (37 Refs)

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5. IMMUNOLOGICAL SPECIFICITY OF NOVIKOFF HEPATOMA CHROMATIN: ISOLATION OF THREE ANTIGENIC PROTEINS.

Stryjecka-Zimmer M, Schmidt WN, Briggs RC, Hnilica LS
Dept. Physiological Chemistry, Medical Sch., Lubartowska 85, 20-123 Lublin, Poland
Int J Biochem; 14(7):591-600 1982

Rabbits immunized with dehistonized Novikoff hepatoma (NH) or normal rat liver (NRL) elicited specific antibodies. Fractionation of nonhistone proteins from the NH group yielded three proteins (approx mol wt 39,000, 49,000 and 56,000) identified with the hepatoma antigenic complexes which showed significant reactivity with PAS staining, suggesting they were glycosylated. Three similar proteins from NRL were PAS negative, and did not react immunologically with antiserum to dehistonized NH chromatin. (49 Refs)

6. MONOCLONAL ANTIBODIES TO HUMAN LUNG TUMOR ANTIGENS DEMONSTRATED BY IMMUNOFLUORESCENCE AND IMMUNOPRECIPITATION.

Brenner BG, Jothy S, Shuster J, Fuks A
(c/o Fuks), McGill Cancer Center, McIntyre Building, 3655 Drummond, Montreal, Quebec H3G 1Y6, Canada
Cancer Res; 42(8):3187-3192 1982

Various studies have demonstrated the usefulness of monoclonal antibodies in recognizing discrete tumor antigenic determinants. The present study describes the tissue reactivity of monoclonal antibodies prepared against a squamous cell carcinoma of the lung. Antigens were purified from the tumor extract by anti-beta2 microglobulin affinity chromatography. These beta2-associated antigens demonstrated tumor specificity by the leukocyte adherence inhibition assay. Antibody-secreting hybridomas were generated by fusion of mouse myeloma cells with mouse spleen cells immunized with purified tumor antigens. Hybridomas were selected by a solid-phase tumor membrane-binding immunoassay. The target specificity of the secreted monoclonal antibodies was ascertained by radioimmunoprecipitation analysis and indirect immunofluorescence on various human tumor and normal tissue sections. Monoclonal antibody-secreting hybridomas 48.4.8 and 48.4.2 secreted immunoglobulin that selectively immunoprecipitated polypeptide fragments from human lung tumor membrane antigens. Hybridoma 9.2.2 secreted antibody that was strongly positive by indirect immunofluorescence on all tested lung squamous cell carcinomas. Adjacent or intervening normal lung tissue did not display significant immunofluorescence. Adenocarcinomas of the lung were negative or focally positive when focal squamous cell differentiation was present. Oat cell carcinomas were negative. The secreted antibody did not significantly stain three extrapulmonary tumors or a variety of normal tissues. (Author abstract) (21 Refs)

7. MOUSE MONOCLONAL ANTIBODY TO A MELANOMA-CARCINOMA-ASSOCIATED ANTIGEN SYNTHESIZED BY A HUMAN MELANOMA CELL LINE PROPAGATED IN SERUM-FREE MEDIUM.

Chee DO, Yonemoto RH, Leong SP, Richards GF, Smith VR, Klotz JL, Goto RM, Gascon RL, Drushella MM
Oncology Lab., Inc., Fiskeville, RI, 02823
Cancer Res; 42(8):3142-3147 1982

A monoclonal antibody, F11, was produced against a tumor-associated antigen from the spent medium of the M14 human malignant melanoma cell line which was grown continuously in serum-free medium. Ouchterlony double-diffusion study revealed that the F11 monoclonal antibody is an immunoglobulin G1. The F11 monoclonal antibody reacted positively with seven of eight (88%) melanoma, five of five (100%) carcinoma, zero of five normal, and zero of two lymphoblastoid cell lines by indirect immunofluorescence test. Also, by indirect immunofluorescence test, F11 monoclonal antibody reacted with cryostat sections from four of five (80%) melanomas, six of seven (86%) carcinomas, zero of one benign nevus, and zero of two benign breast diseases. By the indirect avidin:biotin:peroxidase complex immunoperoxidase method, the F11 monoclonal antibody reacted positively with cryostat sections from five of five (100%) melanomas, five of five (100%) breast cancers, two of two (100%) colon cancers, zero of one benign nevus, and zero of one Hodgkin's disease spleen. Thus, the tumor-associated antigen that the F11 monoclonal antibody recognizes appears to be expressed by melanomas and carcinomas, hence the designation melanoma-carcinoma-associated antigen. Microscopic observations disclosed that the melanoma-carcinoma-associated antigen is present in the cytoplasm, on the membrane of melanoma and carcinoma cells, and in the lumen of glandular structures of breast and colon carcinomas. The mol wt of the melanoma-carcinoma-associated antigen in spent medium from the M14 CEM cell line is 100,000 as determined by sodium dodecyl sulfate: polyacrylamide gel electrophoretic analysis of indirect immunoprecipitates obtained with the F11 monoclonal antibody. (Author abstract) (37 Refs)

8. SERA FROM BREAST CANCER PATIENTS CONTAIN AN IGA ANTIBODY TO A BREAST CYST FLUID COMPONENT.

Witkin SS, Richards JM, Bongiovanni AM, Breed CN, Day NK
Dept. Obstetrics and Gynecology, Cornell Univ. Medical Coll., New York, NY, 10021
Clin Immunol Immunopathol; 23(2):358-365 1982

We have previously demonstrated that aspirated breast cyst fluids from women with benign breast disease contained a particulate component (BCF-PC) that reacted with antiserum to the murine mammary tumor virus (MuMTV). Since women with breast cancer contain antibodies and antigens reactive with MuMTV it was of interest to measure the immune response in breast cancer patients to the BCF-PC. Sera were obtained from breast cancer patients prior to surgery and 5 days postmastectomy, from women with benign breast disease and from healthy women. Analysis for antibody to the BCF-PC was by an enzyme-linked immunosorbent assay. IgA from premastectomy breast cancer patients was significantly more reactive with the BCF-PC than was IgA from women in the other categories (p less than 0.001). In contrast, IgG binding to the BCF-PC did not differ among the various groups. It was further demonstrated that the reactivity of IgA from any particular serum for the BCF-PC remained constant for different BCF-PC isolates. Other fractions of breast cyst fluids were unreactive with IgA from breast cancer patients. Determination of serum IgA levels in these women revealed that the mean IgA level was significantly higher in healthy women than in the other categories (p less than 0.001). Individual IgA levels and levels of IgA antibody to the BCF-PC were found to be not correlated in breast cancer patients. These results indicate that the production of a specific IgA antibody to the BCF-PC increases in sera of patients with breast cancer. Lastly, it was shown that preincubation of patients' sera with disrupted MuMTV, but not intact MuMTV, severely reduced subsequent IgA binding to the BCF-PC. The analysis of sera for IgA antibody to the BCF-PC may be of value for the detection of breast cancer or its recurrence. (Author abstract) (20 Refs)

9. QUANTITATION OF MONOCLONAL ANTIBODY AND ANTIBODY CONJUGATE BINDING TO TUMOUR CELLS USING FLOW CYTOFLUORIMETRY (MEETING ABSTRACT)

Robins RA, Price MR, Baldwin RW
Cancer Research Campaign Laboratories, University of Nottingham, Nottingham NG7 2RD, England
Twenty-third Annual General Meeting of the British Association for Cancer Research, March 29-31, 1982, Edinburgh, Scotland. British Association for Cancer Research 78 pp., 1982.

Monoclonal antibody directly conjugated with fluorescein isothiocyanate has been with a flow cytofluorimeter/sorter (Becton Dickinson FACS IV) to quantitate accurately antibody binding to tumor cells. Directly labelled 791T/36 monoclonal antibody (a mouse antibody against human osteogenic sarcoma cell line 791T) can be detected at a level of 100fg per cell. Cells labelled with antibody can be analyzed without washing, so that the kinetics of labelled antibody association and dissociation, and antibody bound at equilibrium, can be observed directly. The analysis of unlabelled antibody preparations and antibody conjugates (eg drug-antibody, toxin-antibody) can also be performed rapidly and conveniently in competition assays; these methods will detect changes in affinity of conjugated antibodies. In assays using limiting quantities of labelled antibody, solubilized antigen may be detected readily. (no Refs)

10. ANTIBODIES TO INTERMEDIATE FILAMENTS AS DIAGNOSTIC TOOLS: HUMAN GASTROINTESTINAL CARCINOMAS EXPRESS PREKERATIN.

Altmannsberger M, Weber K, Holscher A, Schauer A, Osborn M
(c/o Osborn), Max-Planck-Institute for Biophysical Chemistry, D-3400 Goettingen, W. Germany
Lab Invest; 46(5):520-526 1982

Twenty-five primary gastrointestinal carcinomas have been studied using immunofluorescence microscopy with affinity-purified antibodies to prekeratin and to vimentin. The tissues were alcohol fixed and paraffin embedded before use. In all cases (ie, 1 case of esophageal carcinoma, 7 stomach carcinomas, and 17 large bowel carcinomas) the tumor cells are stained by antibodies to prekeratin. In cases in which only very few tumor cells are present, such as signet ring carcinoma, immunofluorescence with prekeratin antibody provides an easy way to visualize single tumor cells. When the same specimens were tested with antibodies to vimentin, the tumor cells were unstained, and only the fibroblasts and vessels of the stroma were decorated. Four of the tumors were also negative when tested with antibodies specific for either desmin, or glial fibrillary acidic protein or neurofilaments. Three metastases to the abdominal region from tumors originating in the ovary, stomach, and large bowel were like the primary tumors in that the tumor cells were positive when stained with antibodies to prekeratin and negative when tested with the antibodies to vimentin. (Author abstract) (25 Refs)

11. VIL-A1, A MONOCLONAL ANTIBODY REACTIVE WITH COMMON ACUTE LYMPHATIC LEUKEMIA CELLS.

Knapp W, Majdic O, Bettelheim P, Liszka K
Inst. Immunology, Borschkegasse 8A, A-1090 Vienna, Austria
Leuk Res; 6(2):137-147 1982

Generation and characterization of a monoclonal antibody (VIL-A1) raised against Reh cells which specifically reacts with the common acute lymphoblastic leukemia associated (CALL) antigen are described. Immunoelectrophoresis of VIL-A1 showed that the antibody is of the IgM kappa type. Several established human cell lines were tested for their reactivity with VIL-A1 and the reactivity patterns are presented. The reactivity of VIL-A1 with leukemic cells from 97 patients were tested by immunofluorescence. Positive reactions were observed in non-B, non-T acute lymphatic leukemias and in terminal deoxynucleotidyl transferase (TdT) positive chronic myeloid leukemia blast crisis. The reactivity pattern of VIL-A1 and J5 was absolutely identical. VIL-A1 reacted with a membrane component of Reh-6 cells with a mol wt of approx 95,000 daltons. No VIL-A1 reactive component was detected in Raji cells. Not all VIL-A1 antigen bound to lecithin and the binding capacity was heterogenous. Unlabeled VIL-A1 antibody very efficiently blocked the binding of peroxidase-labeled VIL-A1 antibody to a CALL membrane preparation coated on polystyrene tubes. Preincubation with J5 antibody under capping conditions restricted the binding of VIL-A1 antibody, although incubated under non-capping conditions, to one pole of the cell and preincubation with VIL-A1 antibody under capping conditions restricted the binding of J5 antibody to one pole of the cell. Preincubation with negative control antibody had no such effect and left the normal diffuse and ring-staining pattern of both antibodies unchanged. Results showed that the VIL-A1 monoclonal antibody raised against Reh cells reacts with CALL cells but not with normal or malignant B or T lymphocytes. (34 Refs)

12. RAT MONOCLONAL ANTITUBULIN ANTIBODIES DERIVED BY USING A NEW NONSECRETING RAT CELL LINE.

Kilmartin JV, Wright B, Milstein C
Medical Res. Council Lab. Molecular Biology, Cambridge CB2 2QH, England
J Cell Biol; 93(3):576-582 1982

Hybrid myeloma cell lines secreting monoclonal antibodies to tubulin have been prepared using rat myeloma and spleen cells from rats immunized with yeast tubulin. A comparison between the results obtained with the rat myeloma Y3-Ag 1 2 3, which secretes a light chain, and a new line, YB2/O, which does not, shows that they are both excellent parental lines and that the second produces hybrids with no myeloma chain components. The antitubulin antibodies in the serum of rats bearing two of the hybrid myeloma tumors gave titers of up to 1:10(6) from which large amounts of monoclonal antibodies could be easily purified. They recognized tubulin from yeast as well as from birds and mammals. The two antibodies gave clear immunofluorescent staining of yeast mitotic spindles as well as the interphase microtubule network of tissue culture cells. Some difference in the pattern of immunofluorescence staining of yeast cells and nuclei was observed between the two antibodies. The purified antibodies could be conjugated to colloidal gold particles and used for direct labeling of yeast microtubules for electron microscopy. (Author abstract) (36 Refs)

13. MOUSE MONOCLONAL IGM ANTIBODY AGAINST HUMAN LUNG CANCER LINE SK-LC-3 WITH SPECIFICITY FOR H(O) BLOOD GROUP ANTIGEN.

Anger BR, Lloyd KO, Oettgen HF, Old LJ
(c/o Lloyd), Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Hybridoma; 1(2):139-147 1982

Spleen cells of (BALB/c X C57BL6)F1 female mice immunized with SK-LC-3 human lung cancer cells were fused with mouse myeloma line MOPC-2 NSL cells. One hybrid clone was found which produced a monoclonal IgM antibody (F-3) detected with antimouse Ig-major histocompatibility antigen (MHA) and hemagglutination assays. The F-3 hybridoma supernatant reacted with all five lung cancer lines tested (SK-LC-2,-3,-6,-8, and-12), with a renal cancer cell line (SK-RC-7), and with a cervical carcinoma cell line (ME-180). It did not react with melanoma cell line SK-MEL-37. F-3 hybridoma clone was subcloned four times and grown in the nude mouse; it was shown to be producing IgM antibody. F-3 antibody was completely absorbed by O-Type red cells and only partially absorbed by A and B cells; Bombay (Oh) cells were completely ineffective. Direct agglutination tests with F-3 from nude mouse serum showed agglutination of O red cells at a titer of 1:40,000, A2 red cells at a titer of 1:640, and B cells at a titer of 1:80, in all cases much higher than with F-3 supernatants. F-3 was also inhibited by very low concentrations of human H(O) glycoproteins, hog gastric mucin (A + H), a gastric cancer polypeptide, and saliva from an 0 secretor. The high specificity of F-3 for blood group O(H) determinants suggests that it may be useful in hematology and in detection of H(O) determinants in normal and malignant cells. (22 Refs)

14. MONOCLONAL ANTIBODIES DEFINING MARKERS WITH APPARENT SELECTIVITY FOR PARTICULAR HAEMOPOIETIC CELL TYPES MAY ALSO DETECT ANTIGENS ON CELLS OF NEURAL CREST ORIGIN.

Kemshead JT, Fritschy J, Asser U, Sutherland R, Greaves MF
Membrane Immunology Lab., Imperial Cancer Res. Fund, Lincoln's Inn Fields, London WC2A 3PX, England
Hybridoma; 1(2):109-123 1982

Monoclonal antibodies (MAs) were raised against either hemopoietic or neuronal cells, and the extent of sharing of selective expression in different tissue systems was studied. Biochemical data confirmed some of the serological results. Four antigens defined as being present on a subset of hemopoietic cells were also shared with cells of neural crest origin. For example, one MA reacting preferentially with immature (B) lymphoid cells and their corresponding leukemias also bound neuroblastoma, melanoma, and retinoblastoma cell lines. No binding to astrocytoma or medulloblastoma cultured cells was detected by indirect immunofluorescence, however. Other MAs binding hemopoietic cells showed no detectable binding to any neural crest derived cell line. MAs raised against either neuroblastoma cells or human fetal brain produced probes for antigens unique to neural crest cells and for antigens shared with cells in the hemopoietic system. One line, UJ 308, reacted with cells of the myeloid lineage as well as neuroblastoma cells. One antigen on neuroblastoma cells, a 'thymic cortex' 45,000-49,000 mol wt antigen associated with the 12,000 mol wt beta2-like molecule, may be a gene product of the major histocompatibility complex. The extent of cross-reactivity of the present study could be much greater than found between only hemopoietic and neural cells. Nevertheless, the reagents may still be useful for identifying subsets of cells within a population. (41 Refs)

15. MONOCLONAL ANTIBODY AGAINST HUMAN FIBRONECTIN WHICH INHIBITS CELL ATTACHMENT.

Schoen RC, Bentley KL, Klebe RJ
Life Sciences - 3, Los Alamos Natl. Lab., Los Alamos, NM, 87545
Hybridoma; 1(2):99-108 1982

Monoclonal antibodies to fibronectin were raised which specifically inhibited specific biological functions of the fibronectin molecule. Hybridomas constructed between antigen-primed BALB/c mouse spleen cells and the BALB/c mouse myeloma P3-X63-Ag8 were screened. Monoclonal antibodies were isolated that recognized at least nine antigenic determinants of human fibronectin and at least two antigenic determinants of bovine fibronectin. Cross-reactivity of these antibodies with a wide range of mammalian species and sensitivity to various denaturing conditions are reported. (30 Refs)

16. COMPARISON OF THE ENZYME-LINKED IMMUNOSORBENT ASSAY WITH AN EARLY POLYKARYOCYTOSIS INHIBITION ASSAY AND THE AGAR-GEL IMMUNODIFFUSION TEST FOR THE DETECTION OF ANTIBODIES TO BOVINE LEUKEMIA VIRUS.

Graves DC, McQuade M, Weibel K

Dept. Microbiology and Immunology, Univ. Oklahoma Health Sciences Center, PO Box 26901, Oklahoma City, OK, 73190

Am J Vet Res; 43(6):960-966 1982

An indirect enzyme-linked immunosorbent assay (ELISA) was developed, using as test antigen a bovine leukemia virus (BLV) glycoprotein complex (94,000 daltons). The specificity of the ELISA was determined by using specific bovine reference sera. There was a positive reaction using reference sera containing antibodies to BLV, but a negative reaction to reference sera containing antibodies to other ubiquitous bovine agents, ie, bovine viral diarrhea virus (BVDV), foamy-like syncytia virus (BSV), and bovine maedi-like (R-29) virus. The sensitivity of the ELISA for detection of antibodies to BLV was compared with that of the early polykaryocytosis inhibition assay (EPIA), which is based on inhibition of BLV-induced early syncytia formation in cell culture, and with the agar-gel immunodiffusion (AGID) test, using the major glycoprotein (gp51) as antigen. The sera that were tested came from cattle in a high occurrence leukemia herd, cattle in a commercial dairy herd, and from blood samples, obtained from cattle from various parts of Oklahoma, submitted to a diagnostic laboratory for diagnosis of BLV infection. There was 96.2% agreement in the results of all sera tested using the three serotests. The greatest number of positive sera (153) were detected by the EPIA, followed by the ELISA (148) and AGID test (148). There was disagreement in the test results of only 16 sera. Of the 200 sera tested from the commercial dairy herd, 61 (30.5%) were positive by the ELISA, 60 (30%) by the EPIA, and 57 (28.5%) by the AGID test. In the 111 sera from the diagnostic laboratory, 45 (40.5%) were positive by the ELISA, 45 (40.5%) by the EPIA, and 47 (42.3%) by the AGID test. With the 102 sera from the high occurrence leukemia herd, 42 (41.2%) were positive by the ELISA, 48 (47%) by the EPIA, and 44 (43.1%) by the AGID test. The indirect ELISA is another serotest that can be used for the diagnosis of BLV infection in cattle. It is specific, equally as sensitive as the AGID test, rapid to perform requiring inexpensive equipment, and may be the preferred serotest for screening large numbers of animals for BLV infection. (Author abstract) (30 Refs)

TUMOR ANTIBODIES ASSOCIATED WITH VIRUSES

17. PROTECTION OF NEONATAL MICE AGAINST HERPES SIMPLES VIRUS INFECTION: PROBABLE IN VIVO ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY.

Kohl S, Loo LS
Univ. Texas, P.O. Box 20708, Houston, TX, 77025
J Immunol; 129(1):370-376 1982

Infant mice are extremely susceptible to fatal Herpes simplex virus (HSV) infection. They are unable to produce antibody to HSV, and their leukocytes cannot mediate antibody-dependent cellular cytotoxicity (ADCC) to HSV-infected cells. In order to avoid H-2-dependent effector mechanisms and instead analyze possible in vivo ADCC, a murine model employing adoptive transfer of antibody and human leukocytes was developed. Administration of either human immune globulin or leukocytes ip from HSV immune or nonimmune humans could not protect infant C57BL/6 mice from fatal HSV infection. In contrast, a combination of a subneutralizing dilution of globulin and leukocytes from nonimmune or immune human donors, given 1 day before inoculation, was highly protective against lethal HSV infection. The cells involved included lymphocytes or monocyte-macrophages. At least 5 x 10(6) viable leukocytes (or 1 x 10(6) monocyte-macrophages) and immune serum globulin concentrations as low as 10(-8) were protective. Infected cell monolayer adsorption and DEAE column fractionation demonstrated that the protection by globulin was due to specific antiviral IgG antibody. Protection was not seen in animals receiving virus before immune transfer. Protection did not involve synergistic viral neutralization by antibody and cells, as shown by in vitro experiments. Animals receiving globulin and cells, unlike normal infant mice, had circulating antiviral antibody and peritoneal leukocytes able to mediate ADCC to HSV-infected cells. This is the first in vivo evidence for the role of human ADCC. This model also allows for the in vivo evaluation of the ability of cells from immunocompromised humans to curb viral infection. (Author abstract) (72 Refs)

18. AN OUTBREAK OF PNEUMOCYSTIS CARINII PNEUMONIA IN HOMOSEXUAL MEN.

Follansbee SE, Busch DF, Wofsy CB, Coleman DL, Gullet J, Aurigemma GP, Ross T, Hadley WK, Drew WL
Dept. Medicine, Univ. California, San Francisco, CA, 94143
Ann Intern Med; 96(6,part1):705-713 1982

Pneumocystis carinii pneumonia has rarely been reported in previously healthy persons over the age of 6 mo. Five cases of P carinii pneumonia in adult homosexual men, confirmed by biopsy results, are reported. All five patients were seropositive when tested for antibodies to cytomegalovirus and four had evidence of active concurrent cytomegalovirus infections. Kaposi's sarcoma was shown in two of the patients and one had possible Pneumocystis infection of the central nervous system as well as P carinii pneumonia. Three patients had second episodes of Pneumocystis pneumonia. Four of the five patients have died. Past or concurrent cytomegalovirus infection and homosexuality were the only common epidemiologic features in all five patients. (Author abstract) (57 Refs)

19. DISSEMINATED KAPOSI'S SARCOMA IN HOMOSEXUAL MEN.

Friedman-Kien AE, Laubenstein LJ, Rubinstein P, Buimovici-Klein E, Marmor M, Stahl R, Spigland I, Kim KS, Zolla-Pazner S
New York Univ. Medical Center, 530 First Ave., New York, NY, 10016
Ann Intern Med; 96(6,part1):693-700 1982

Nineteen cases from an epidemic of disseminated Kaposi's sarcoma in homosexual men were studied by clinical, virologic, immunologic, and genetic methods. The patients were all male homosexuals ranging in age from 29 to 52 yr, with histories of multiple sexually transmitted diseases and exposure to both prescription and recreational drugs. Sites of disease included skin (16 of 19 patients), lymph nodes (13 patients), gastrointestinal tract (12 patients), spleen (3 patients), and lung (1 patient). Most patients had elevated levels of serum immunoglobins, positive antibody titers to hepatitis A and B virus, cytomegalovirus and Epstein-Barr virus, and impairment of cell-mediated immunologic reactions. The frequency of HLA-DR5 in these patients was significantly elevated. Two of the 19 patients died. Although the precise cause of this epidemic is unknown, it is likely that a genetic predisposition, an acquired immunoregulatory defect, and one or more infectious agents and drugs may be involved. (Author abstract) (48 Refs)

20. MONOCLONAL ANTIBODIES TO THE P21 PRODUCTS OF THE TRANSFORMING GENE OF HARVEY MURINE SARCOMA VIRUS AND OF THE CELLULAR RAS GENE FAMILY.

Furth ME, Davis LJ, Fleurdelys B, Scolnick EM
Lab. Tumor Virus Genetics, NCI, Bethesda, MD, 20205
J Virol; 43(1):294-304 1982

We have isolated eight rat lymphocyte-myeloma hybrid cell line producing monoclonal antibodies that react with the 21,000-dalton transforming protein (p21) encoded by the v-ras gene of Harvey murine sarcoma virus (Ha-MuSV). These antibodies specifically immunoprecipitate both phosphorylated and non-phosphorylated forms of p21 from lysates of cells transformed by Ha-MuSV. All eight react with the products of closely related ras genes expressed in cells transformed by two additional sarcoma viruses (rat sarcoma virus and BALB sarcoma virus) or by a cellular Harvey-ras gene placed under the control of a viral promoter. Three of the antibodies also react strongly with the p21 encoded by the v-ras gene of Kirsten MuSV. These same three antibodies immunoprecipitate the predominant p21 species synthesized normally in a variety of rodent cell lines, including the p21 produced at high levels in 416B murine hemopoietic cells. This suggests that an endogenous gene closely related to Kirsten-ras is expressed in these cells. The monoclonal antibodies have been used to confirm two properties associated with p21: localization at the inner surface of the membrane of Ha-MuSV-transformed cells, assayed by immunofluorescence microscopy, and binding of guanine nucleotides. (Author abstract) (42 Refs)

21. HEPATITIS-B VIRUS INFECTION IN BLACK CHILDREN WITH HEPATOCELLULAR CARCINOMA.

Kew MC, Hodkinson J, Paterson AC, Song E
Dept. Medicine, Witwatersrand Univ. Medical Sch., Hospital Hill, Johannesburg 2001, South Africa
J Med Virol; 9(3):201-207 1982

Six unselected South African black children (2 female, 15 and 16 yr old; 4 male, 10-13 yr old) with hepatocellular carcinoma (HCC) were examined for hepatitis-B virus (HBV) infection. Characteristics of the tumors were similar to those in black adults. All of the patients were positive for hepatitis B surface (HBs) antigen and hepatitis B core antigen in the serum. Hepatitis Be antigen was present in four patients; sera from the two patients without e antigen (1 male, 1 female) were positive for e antibody. All of the sera were negative for HBs antigen. Taken in conjunction with the HBV status of black adults in South Africa, the findings suggest the possibility that nearly all black patients with HCC are or have been infected with HBV. If HBV is oncogenic, tumor formation may occur within 10 yr of the initial infection. (14 Refs)

22. CHARACTERIZATION OF DUALTROPIC TYPE C RETROVIRUSES ISOLATED FROM SPONTANEOUS NON-T LYMPHOMAS OF SJL/J(V+) MICE.

De Rossi A, D'Andrea E, Chieco-Bianchi L
Laboratorio di Oncologia, Istituto di Anatomia Patologica, Via Gabelli 61, 35100 Padova, Italy
Tumori; 68(2):95-104 1982

Endogenous XC- viruses were isolated from non-T spontaneous lymphomas of SJL/J(v+) mice. These isolates were cloned by limiting dilution procedure and characterized for biological and immunological properties. At the electron microscope these isolates showed typical retrovirus Type C morphology. Reverse transcriptase and immunofluorescence assays showed that these viruses were infectious for mouse and heterologous cell lines. Since some of the isolates induced cytopathic foci in mink lung cultures, they had properties similar to those described for other recombinant dualtropic viruses. Using a panel of monoclonal antibodies against gp 70 and p 15 (E) viral proteins, it was observed that the dualtropic XC- viral isolates had an antigenic profile different from that of SJL ecotropic XC+ virus. (Author abstract) (37 Refs)

23. CELL-MEDIATED AND HUMORAL IMMUNE RESPONSES OF RATS DURING THE PROGRESSION OF PRIMARY AVIAN SARCOMA VIRUS-INDUCED INTRACEREBRAL GLIOMAS (MEETING ABSTRACT)

Woosley RE, Watkins PJ, Mahaley MS
No affiliation given
1982 Annual Meeting of the American Association of Neurological Surgeons, April 25-29, 1982, Honolulu, Hawaii. American Association of Neurological Surgeons 234 pp., 1982.

The avian sarcoma virus-induced glioma tumor model in the Fischer 344 rat has shown many parallels to the human glioma response. A longitudinal study of the specific immune responses of this tumor model has been studied using an in vitro microcytotoxicity assay monitoring cellular, humoral and antibody-dependent cytotoxicity. These studies were carried out to identify if and when an immune response might occur as the animal developed his tumor so that these responses might be manipulated in future therapeutic protocols. Tumor-bearing animals and their age-matched controls were sacrificed and studied every two weeks, from three to twenty-five weeks after they had been injected intracereberally with avian sarcoma virus at age day five. Other animals were immunized with target tumor cells to serve as an internal cytotoxicity control. Specific cellular (average 12%), humoral (average 5%) and antibody-dependent (average 11%) cytotoxicity of the tumor-bearing animals was not significantly different from their age-matched controls averaging 15%, 5%, and 13%, respectively. Immunized animals showed a significant specific cellular and humoral response averaging 30% and 39% respectively. (no Refs)

24. ANTIBODIES TO ADULT T-CELL LEUKEMIA-VIRUS-ASSOCIATED ANTIGEN (ATLA) IN SERA FROM PATIENTS WITH ATL AND CONTROLS IN JAPAN: A NATION-WIDE SERO-EPIDEMIOLOGIC STUDY.

Hinuma Y, Komoda H, Chosa T, Kondo T, Kohakura M, Takenaka T, Kikuchi M, Ichimaru M, Yunoki K, Sato I, Matsuo R, Takiuchi Y, Uchino H, Hanaoka M
Inst. Virus Res., Kyoto Univ., Kyoto 606, Japan
Int J Cancer; 29(6):631-635 1982

A nation-wide sero-epidemiologic survey of adult T-cell leukemia virus (ATLV), detected as anti-ATLA (ATLV-associated antigen), was made in Japan. Sera from adult donors in 15 different locations were screened for anti-ATLA. High incidences (6 to 37%) of antibody-positive donors were found in seven regions, one in northern Japan, and the others in southwestern regions. These areas are ATLV-endemic areas corresponding to ATL-endemic areas. Examination of sera from healthy donors aged 6 to 80 yr in ATL-endemic areas showed an age-dependent increase of seropositive donors with a maximum of about 30% to 40 yr of age. Anti-ATLA was found in all but two of 142 patients with ATL. Anti-ATLA-positive patients with ATL were mainly found in ATLV-endemic areas and only a few in ATL-nonendemic areas. Six patients with cutaneous T-cell lymphoma in ATLV-nonendemic areas gave a negative reaction for anti-ATLA. The geometric mean titer of anti-ATLA of patients with ATL was higher than that of healthy donors. (Author abstract) (9 Refs)

25. HERPES GESTATIONIS ASSOCIATED WITH CHORIOCARCINOMA.

Slazinski L, Degefu S
Sarasota, FL
Arch Dermatol; 118(6):425-428 1982

Herpes gestationis (HG) is a rare, vesicobullous dermatosis of pregnancy or the puerperium. It has been associated with hydatid mole and the use of oral contraceptives. Reports of HG and choriocarcinoma are extremely rare; only two cases have been reported. Metastatic choriocarcinoma, followed by a pruritic, bullous eruption, developed in a 36-yr-old woman. A biopsy specimen of the lesions showed subepidermal bullae, with an eosinophilic infiltrate. Direct immunofluorescent microscopic findings showed IgG and C3 deposition at the basement membrane zone, establishing the diagnosis of HG. Methotrexate therapy produced a cure of the carcinoma and a simultaneous resolution of the skin lesions. To our knowledge, this is the first report of the association of HG and choriocarcinoma with immunofluorescent microscopic findings. (Author abstract) (30 Refs)

26. EVOLUTION OF INFECTIOUS MONONUCLEOSIS INTO EPSTEIN-BARR VIRUS CARRYING MONOCLONAL MALIGNANT LYMPHOMA.

Abo W, Kamada M, Motoya T, Aya T, Nakao T, Takada K, Imamura M, Iwanga M, Yano S, Osato T
(c/o Osato) Dept. Virology, Cancer Inst., Hokkaido Univ. Sch. Medicine, Sapporo 060, N15 W7, Japan
Lancet; 1(8284):1272-1276 1982

A monoclonal malignant lymphoma was diagnosed in a 30-mo-old Japanese boy, who, since the age of 12 mo, had had chronic, recurrent infectious mononucleosis manifested by repeated episodes of severe cough and high fever accompanied by marked lymphadenopathy and hepatosplenomegaly and high serum Epstein-Barr virus (EBV) antibody titers. The diagnosis of Burkitt's lymphoma was made when a cervical lymph-node biopsy specimen revealed massive proliferation of immature B-cells with starry-sky histiocytes. These lymph-node cells were characterized by a translocation between chromosomes 10 and 17. There were approx 9 EBV genome-equivalents per cell. Most cells were positive for nuclear antigen (EBNA); early antigen (EA) and viral capsid antigen (VCA) were also detected. The presence of EBV was supported by the finding that the cell-free lymph-node extract transformed cord-blood lymphocytes into EBNA-positive blast cells. The proportion of EA-positive and VCA-positive cells increased rapidly in culture for 24 hr, then the positive cells degenerated rapidly and completely. The cells also contained numerous herpes-type virus particles. The child improved considerably with cytostatic treatment and has been in remission for 2 yr. (Author abstract) (23 Refs)

ANTITUMOR ACTIVITY AND IMMUNOTHERAPY

27. PRETREATMENT OF DONOR BONE MARROW WITH MONOCLONAL ANTIBODY OKT3 FOR PREVENTION OF ACUTE GRAFT-VERSUS-HOST DISEASE IN ALLOGENEIC HISTOCOMPATIBLE BONE-MARROW TRANSPLANTATION.

Filipovich AH, Ramsay NK, Warkentin PI, McGlave PB, Goldstein G, Kersey JH
Dept. Pediatrics, Univ. Minnesota Hosp., Box 261, Mayo, Minneapolis, MN, 55455
Lancet; 1(8284):1266-1269 1982

Ten consecutive patients undergoing transplantation of bone marrow from histocompatible siblings for treatment of hematological malignancy took part in a pilot study to test the safety of in vitro treatment of donor bone marrow with monoclonal antibody OKT3. Three male and seven female patients aged 7-34 yr received concentrated bone-marrow buffy-coat cells which had been incubated with OKT3 before infusion. In-vitro studies confirmed that almost all immunocompetent T lymphocytes in the bone-marrow samples were coated with OKT3 at the time of infusion. In vitro, neonatal rabbit complement inhibited the proliferation of bone-marrow T lymphocytes in samples preincubated with OKT3 to less than 4% of the mitogenic responses of the untreated bone marrow. In contrast, fresh autologous complement did not effectively lyse OKT3-treated bone-marrow cells. Infusion of OKT3-treated bone marrow was safely accomplished, and engraftment was achieved in all patients (mean 23 days). Nine of 10 patients survived for more than 100 days after bone-marrow transplantation, but significant acute graft-versus-host disease (GvHD) requiring treatment with steroids developed in 5 of the 10. This finding suggests that further modifications for bone-marrow pretreatment will be needed to achieve effective prophylaxis against acute GvHD in histocompatible bone-marrow transplantation. (Author abstract) (17 Refs)

28. MONOCLONAL ANTIBODY TO HUMAN COLON CARCINOMA THAT INHIBITS NATURAL KILLER ACTIVITY (MEETING ABSTRACT).

Allen J, Ferrone S, Boue D, Kay N
Veterans Administration Center and University of Minnesota, Minneapolis, MN
Gastroenterology; 82(5,part2):1007 1982

Using monoclonal antibodies (MA) a variety of new surface antigens on tumor cells have been described. We have been interested in further defining surface antigens on colon cancer cells and exploiting these antigens to enhance host defense mechanisms. Since cells alter their surface antigens during In Vitro culture, we used fresh colon cancer tissue to develop 6 MA reactive with colon cancer cells. We report on one such MA: CJA-3. CJA-3 fixes complement, binds Staph protein A (SPA) and is an IgG3 MA which reacts equally with 4 (of 4) colon cell lines. CJA-3 also reacts with several other solid tumor lines but not lymphoid cell lines, normal lymphocytes, or normal gastric, duodenal and colonic mucosa. Most antibodies enhance cell mediated tumor lysis, but suprisingly, CJA-3 inhibited lysis of colon cell lines. Colon cancer line SW-620 is sensitive to Natural Killer (NK) lysis but concurrent addition of CJA-3 to NK + 620 inhibited lysis by 33% (16 hr assay). Treatment of 620 with CJA-3 (16 hrs) pre NK assay, lowered NK lysis by 23%. CJA-3 + 620 (1 hr), or CJA-3 + NK cells (16 hrs) did not alter NK activity. In addition, we again pretreated 620 with similar dilutions of CJA-3 for 16 hours. Treated cells bound 31% less SPA than untreated cells or cells pretreated for 1 hour. This probably indicates a time dependent modulation of CJA-3 antigen as a result of antibody binding. (no Refs)

29. NEURONAL ORIGIN OF HUMAN ESTHESIONEUROBLASTOMA DEMONSTRATED WITH ANTI-NEUROFILAMENT MONOCLONAL ANTIBODIES.

Trojanowski JQ, Lee V, Pillsbury N, Lee S
Div. Neuropathology, Dept. Pathology and Laboratory Medicine, Univ. Pennsylvania Sch. Medicine, Johnson Pavillion G/2, Philadelphia, PA, 19104
N Engl J Med; 307(3):159-161 1982

Neuronal origin of esthesioneuroblastoma (ENB) diagnosed in a 78-yr-old woman who was admitted to the hospital because of recurrent epistaxis and nasal obstruction is discussed. Findings showed that human ENB cells contain intermediate filaments, as do other neoplastic and non-neoplastic mammalian cells. The presence of neurofilament proteins in the cells was demonstrated. In contrast, two other intermediate filaments present in the brain (vimentin and glial filaments) were not present in the tumor cells. Data provided strong evidence of the neuronal origin of ENB, since neurofilament proteins have been described only in neurons and neuronal cell lines. (12 Refs)

30. STUDY OF HUMAN MELANOMA CELL SURFACE ANTIGENS USING MONOCLONAL ANTIBODIES.

Yeh MY
University of Washington, Seattle, WA
Diss Abstr Int [B]; 42(12,pt1):4742-B 1982

BALB/c mice were immunized with cultivated cells from one of two melanomas, M1804 or SK-MEL 28. Spleen cells from hyperimmunized mice were fused with mouse NS-1 myeloma cells. Hybrid cells were grown in HAT (hypoxanthine, aminopterin, thymidine) selective medium and screened for production of antibodies that bound to melanoma cells but not to autologous skin fibroblasts. Five hybrids were selected for extensive studies. Three hybridomas, 3.1, 3.2, and 3.3 form monoclonal antibodies to the same antigenic determinant, called 3.1 which is strongly expressed by the immunizing melanoma, M1804. Binding assays performed with a large panel of cultured human cells have demonstrated that antigen 3.1 is expressed strongly by a small subgroup of cultured melanomas, less strongly by another group of melanomas or not at all by a third group of melanomas. It is not detected on cultures from most non-melanoma tumors, normal skin fibroblast lines, or on B- or T-cells lines. Hybridomas 4.1 and 4.2 were generated against melanoma line SK-MEL 28. Hybridoma 4.1 produces an IgG antibody which identifies a cell surface protein with a molecular weight of 97,000. This protein, designated p97, is strongly expressed by both cultured cells and biopsy material from melanomas and certain other tumors. Cells from various normal tissues express only low amounts of p97. Hybridoma 4.2 secretes an IgM antibody which recognizes an antigen shard by about 95% of melanoma lines and 25% of cultured non-melanoma tumors tested. (no Refs)

31. IMMUNOPEROXIDASE STAINING OF CARCINOEMBRYONIC ANTIGEN WITH MONOCLONAL ANTIBODIES IN ADENOCARCINOMA OF THE COLON.

Lindgren J, Wahlstrom T, Bang B, Hurme M, Makela O
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Histochemistry; 74(2):223-227 1982

Application of monoclonal antibodies to the immunoperoxidase staining of carcinoembryonic antigen (CEA) is described. A distinct positive staining of the neoplastic epithelial cells was seen in all sections stained with unadsorbed anti-CEA ascites fluids and the rabbit anti-CEA-antiserum. All controls including the ascites fluids adsorbed with purified CEA were negative. The nonspecific background staining of the ascites fluids was negligible in all dilutions used giving a better distinction than the rabbit antiserum. (9 Refs)

32. DETECTION OF A COMMON ANTIGEN ON MURINE B CELLS AND LYT-2+ T CELLS BY A RAT MONOCLONAL ANTIBODY, 14D10.

Kung JT, Sharrow SO, Mage MG, Paul WE
Lab. Immunology, NIH, Natl. Inst. Allergy and Infectious Diseases, Building 10, Room 11N311, Bethesda, MD, 20205
J Immunol; 129(1):81-86 1982

This paper reports the production of a rat monoclonal antibody, 14D10, which recognizes a determinant shared between B cells and Lyt-2+ T cells. Three subpopulations of spleen cells were defined based on the density of bound 14D10. They have been designated 14D10-SP (strongly positive), 14D10-WP (weakly positive), and 14D10-N (negative). Dual parameter immunofluorescence studies showed that 90% of 14D10-SP cells are IgM+ cells and more than 92% IgM+ cells are 14D10-SP. Of 14D10-WP cells, approx 60% are Lyt-1+2+ T cells and less than 10% are Igm+ cells. However, most (greater than 90%) of Lyt-2+ T cells are reactive with 14D10. Staining of purified populations of Lyt-2+ and Lyt-2(-) T cells with fluoresceinated 14D10 also showed greater than 90% of Lyt2+ T cells to be 14D10+, and fewer than 10% of Lyt-2(-) T cells are 14D10+. Mouse thymus contained very few (approx = 5%) 14D10+ cells. Analysis of bone marrow cells shows almost all small cells to be 14D10+. Six Abelson virus-transformed cell lines all express the antigen recognized by 14D10. (Author abstract) (19 Refs)

33. FURTHER POLYMORPHISM OF THE TLA LOCUS DEFINED BY MONOCLONAL TL ANTIBODIES.

Shen FW, Chorney MJ, Boyse EA
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Immunogenetics; 15(6):573-578 1982

Six new monoclonal TL antibodies are described. At least one new TL antigen is defined (TL.7), and at least one more Tla allele, bringing the total number of known Tla alleles to six. Five of the monoclonal antibodies, and probably all six, identify distinct TL antigenic specificities. Four of these antigens conform in strain distribution and expression on leukemia cells to antigens defined by conventional antisera. The data contain a hint that monoclonal TL antibodies like TL.m6 may serve to identify a region of the Tla gene, which determines whether or not prothymocytes will respond to physiological induction by expressing TL, and thus may provide a means to study the regulatory mechanism that determines whether mouse strains are phenotypically TL+ or TL-. (Author abstract) (14 Refs)

34. ENHANCED SUSCEPTIBILITY OF GLUTARALDEHYDE-TREATED TUMOR CELLS TO ANTIBODY-DEPENDENT MACROPHAGE-MEDIATED CYTOLYSIS.

Iwata-Dohi N, Esumi-Kurisu M, Ikenami M, Sadatsune K, Mizuno D, Yamazaki M

(c/o Esumi-Kurisu), Teikyo Univ., Sagamiko, Kanagawa 199-01, Japan

Cancer Res; 42(8):3196-3200 1982

The effect of treatment of target tumor cells with glutaraldehyde (GA) on antibody-dependent macrophage-mediated cytolysis was investigated in a C3H/He mouse-MM46 syngeneic tumor system. GA-treated tumor cells were more susceptible to antibody-dependent macrophage-mediated cytolysis. Lysis of GA-treated cells was observed with less antibody and fewer macrophages than that of untreated cells. However, GA-treated cells had the same amount of antigen sites and the same activity of antibody-dependent attachment to macrophages as do fresh tumor cells. Thus, this enhancement of lysis did not occur at the antibody-binding step or the early step of contact between macrophages and tumor cells but at the subsequent step, perhaps at the tumor lysis step. GA-treated tumor cells could not synthesize DNA or RNA, but cells attenuated with mitomycin C or actinomycin D were not susceptible to antibody-dependent macrophage-mediated cytolysis. These results suggest that the cytostatic effect of GA does not involve change in susceptibility of target cells to lysis, but some impairment of the cell membrane. GA-treated tumor cells could not grow in vivo and could induce antitumor immunity. (Author abstract) (20 Refs)

35. USE OF MONOCLONAL ANTIBODIES IN DETECTION OF MELANOMA-ASSOCIATED ANTIGENS IN INTACT HUMAN TUMORS.

Thompson JJ, Herlyn MF, Clark WH, Elder DE, Steplewski Z, Koprowski H

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Am J Pathol; 107(3):357-361 1982

The use of antimelanoma monoclonal antibodies on tissue sections using a two-step indirect immunoperoxidase technique is reported. Antibodies 691-13-17 and 691-I5-Nu4B reacted with dysplastic nevus cells and all melanomas tested, but not with normal skin melanocytes, intradermal nevi, or lentigines. Antibody 691-13-17, directed against DR antigen, reacted also with Langerhan's cells, macrophages, and a subpopulation of lymphocytes. Antibody 691-I5-Nu4B reacted only with melanomas. The technique allows analysis of the expression of antigens by tumor cells in situ. (Author abstract) (11 Refs)

36. SELECTIVE BLOCKADE OF HUMAN NATURAL KILLER CELLS BY A MONOCLONAL ANTIBODY.

Newman W
Program in Basic Immunology, Fred Hutchinson Cancer Res. Center, Seattle, WA, 98104
Proc Natl Acad Sci USA; 79(12):3858-3862 1982

A murine monoclonal antibody, 13.1, which blocks human natural killer (NK) cell-mediated lysis, has been developed. Hybridoma 13.1 was derived by fusion of NS-1 cells with spleen cells from mice immunized with an enriched population of NK cells. Supernatants of growing hybridomas were screened for their ability to block NK cell-mediated lysis of K562 targets. Antibody 13.1 is an IgG1 with a single light chain type and it does not fix complement. The 13.1 antigen is expressed on all peripheral blood mononuclear cells, with an antigen density approx 1/30th that of HLA antigen heavy chain. Pretreatment and washing experiments revealed that inhibition of cytotoxicity occurred at the effector cell level only. Significant blocking was achieved with nanogram quantities of antibody and was not due to toxic effects on NK cells. Likewise, controls with other antibodies of the same subclass demonstrated that blocking was not a consequence of mere binding to NK cells. When a panel of 17 NK cell-susceptible targets was tested, the lysis of only 5 of these was blocked, namely K562, HL-60, KG-1, Daudi, and HEL, a human erythroleukemic cell line. The lysis of 12 human B cell and T cell line targets was not inhibited. In addition to the demonstration that the 13.1 antigen is a crucial cell surface structure involved in NK lysis, a heterogeneity of target cell recognition has been revealed that argues for the proposition that individual NK cells have multiple recognitive capabilities. (Author abstract) (28 Refs)

37. A MONOCLONAL ANTIBODY (MMA) THAT IDENTIFIES A DIFFERENTIATION ANTIGEN ON HUMAN MYELOMONOCYTIC CELLS.

Hanjan SN, Kearney JF, Cooper MD
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Clin Immunol Immunopathol; 23(2):172-188 1982

A monoclonal IgMkappa antibody (MMA) was produced against the human histocytic cell line, U-937. This antibody reacted by indirect immunofluorescence and complement-mediated lysis with adherent mononuclear cells and granulocytes. MMA was unreactive with circulating T and B cells, erythrocytes, and platelets. Depletion of MMA+ cells from blood mononuclear cell populations significantly reduced the reactivity of these cells to antigens and mitogens. The lymphoproliferative responses were restored by addition of 10% MMA+ cells. MMA is expressed by some T-cell lines (HSB-2, MOLT-3, MOLT-4) and mitogen-activated T cells, but not by B-cell lines or activated B cells. Studies using double immunofluorescence showed that 80% of activated T4+ and 10% of T8+ cells expressed MMA. The antigen is present on precursors of in vitro granulopoietic colony-forming cells. Malignant cells from patients with both acute and chronic myeloid leukemias express this antigen. The MMA antibody thus defines a unique differentiation antigen present on human myeloid cells, their precursors, and a subpopulation of activated T cells. (Author abstract) (45 Refs)

38. HETEROGENEITY OF MELANOMA-ASSOCIATED ANTIGENS DETECTED BY SERA FROM PATIENTS RECEIVING ADJUVANT ALLOGENEIC TUMOR VACCINE IMMUNOTHERAPY.

Dent PB, McCulloch PB, Liao SK, Stone BR, Singal DP
Dept. Pediatrics, Internal Medicine and Pathology, McMaster Univ., Ontario Cancer Treatment and Res. Foundation, Hamilton Clinic, Hamilton, Ontario L8N 3Z5, Canada
Clin Immunol Immunopathol; 23(2):379-391 1982

Sera from 40 patients with malignant melanoma entered into a randomized controlled trial of nonspecific and specific active immunotherapy were studied for the presence of melanoma-specific IgG antibody. Reactivity was revealed by mixed hemadsorption assay against a panel of 10 cultured melanoma cell lines. Prior to therapy 3 of 40 patients had antibody to one or more melanoma lines which in all cases was eliminated by absorption with platelets or colon carcinoma cells. After 6 mo of therapy patients in the group not receiving tumor vaccine had no absorption-resistant antimelanoma reactivity. However all 10 patients receiving allogeneic tumor vaccine had high titered melanoma reactivity which in 8 patients was not removed by platelet or carcinoma absorption. Three patients reacted only against melanoma targets while of the remaining five patients, four reacted against cultured brain tumor cells supporting previous suggestions of a possible antigenic cross-reactivity among tumors of neuroectodermal origin. Clinical outcome was not correlated with the presence of antibody to melanoma target cells. Persistance of antibody was dependent on continued vaccine administration suggesting that rather than being an index of resistance, the presence of antibody may be a marker for the presence of tumor. Sera from alloimmunized melanoma patients identify a heterogeneous complex of melanoma-associated surface antigens. More information about the serological and immunological properties of these antigens is required to determine if these responses are clinically relevant. (Author abstract) (21 Refs)

39. THE EFFECT OF MONOCLONAL ANTIBODY-DIRECTED IMMUNOTOXINS AND IMMUNOMODULATORS ON CULTURED OSTEOGENIC SARCOMA CELLS (MEETING ABSTRACT)

Embleton MJ, Flannery GR, Pelham J, Rowland GF, Pihl A, Baldwin RW
Cancer Research Campaign Laboratories, University of Nottingham, Nottingham, England
Twenty-third Annual General Meeting of the British Association for Cancer Research, March 29-31, 1982, Edinburgh, Scotland. British Association for Cancer Research 78 pp., 1982.

A monoclonal antibody (MoAb) raised against an osteogenic sarcoma cell line, 791T, was conjugated to various cytotoxic drugs and toxins, and to Lymphoblastoid Interferon (IFN) mainly using N-succinimidyl-3-(2-pyridyldithio)-proprionate. Conjugates were tested for cytotoxic properties on 791T and several other cross-reactive osteogenic sarcoma cell lines using radioisotopic assays to measure protein or DNA synthesis. Virtually all immunotoxin conjugates retained antibody binding activity for 791T cells; in most, cytotoxic activity was lost or diminished compared with the unconjugated agent. The least inactivated were Vindisine/MoAb and Ricin A chain/MoAb, for which the LD50 values were approximately 100-fold and 30-fold less than the parent compounds respectively. IFN/Moab conjugates did not directly affect the cells, but IFN alone also had only a marginal cytostatic effect. However, IFN/MoAb was highly effective in stimulating natural killer (NK) cell activity against 791T and other target cells. 791T cells, but not antigenically unrelated cells, preincubated with the conjugate induced activation of NK cells against 51Cr-labelled third party cells in mixed culture. These studies indicate that further development is required for the preparation of immunotoxins, but suggest an alternative approach towards antitumor therapy using indirectly acting MoAb-directed immunomodulators. (no Refs)

40. BIOLOGICAL ACTIVITY OF A MONOCLONAL ANTIBODY SPECIFIC FOR A RAT SARCOMA (MEETING ABSTRACT)

North SM, Dean CJ
Institute of Cancer Research, Clifton Avenue, Sutton, Surrey, SM2 5PX, England
Twenty-third Annual General Meeting of the British Association for Cancer Research, March 29-31, 1982, Edinburgh, Scotland. British Association for Cancer Research 78 pp., 1982.

A monoclonal antibody, (M10/76) of IgG2 isotype, directed against a tumor associated antigen of the chemically induced rat fibrosarcoma, MC24, is being used to investigate the role of humoral immunity in metastatic disease. To assess the biological activity of M10/76 in vivo, affinity purified antibody was injected iv into immunocompetent rats immediately before an iv challenge with viable tumor cells. After 16 days the animals were sacrificed and the number of lung colonies estimated. Lungs from the control groups had large numbers of tumor colonies, whereas lungs from animals treated with specific antibody contained no visible tumor colonies. Antibody M10/76 was also examined for its effects on spontaneous metastases in vivo. MC24 was grown in the hind limb of congenitally athymic male rats for 21 days and then removed by amputation of the hind limb. Specific antibody was administered iv at a dose of 50ug/rat given on alternate days throughout tumor growth and until 75 days post-amputation. The animals were then killed and examined for metastases. While all control animals showed metastases either to lung or lymph nodes, those treated with M10/76 showed either no metastatic lesions or enhanced metastatic disease. We conclude that Ab M10/76 is biologically active in vivo and is capable of influencing the course of metastatic disease. (no Refs)

41. REACTIVITY OF MONOCLONAL ANTIBODIES PRODUCED AGAINST HUMAN LUNG CANCER CELL LINES (MEETING ABSTRACT)

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Twenty-third Annual General Meeting of the British Association for Cancer Research, March 29-31, 1982, Edinburgh, Scotland. British Association for Cancer Research 78 pp., 1982.

A panel of monoclonal antibodies was produced by fusion of sensitized murine spleen cells with the NS-1 myeloma, against several human lung carcinoma cells including the E14 and BEN lines (squamous cell carcinoma). The majority of the monoclonal probes, tested by radioimmunoassay, recognized species-specific antigens or lung differentiation antigens. However several of the antibodies exhibited reactivity against target antigens with a more restricted distribution. Antibodies designated 7B3.5, 7B5.4 + and 7B17.7 were reactive with a variety of human carcinoma cell lines derived from several different tissues but were negative against several normal lung lines. Two monoclonal antibodies (7B24.4, 7BC9.1) recognized a target antigen found only on the immunizing cell line (BEN) and in the case of 7BC9.1 at a much lower density on one colorectal carcinoma cell line (W1DR). These antibodies should prove useful for the definitive characterization of putative human tumor associated antigens in lung and other cancers. (no Refs)

42. SELECTIVE KILLING OF MALIGNANT CELLS IN A LEUKAEMIC RAT BONE MARROW USING AN ANTIBODY-RICIN CONJUGATE.

Thorpe PE, Mason DW, Brown AN, Simmonds SJ, Ross WC, Cumber AJ, Forrester JA
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Nature; 297(5867):594-596 1982

A model system in which lethally irradiated PVG rats were injected with a mixture of bone marrow cells and leukemic cells and in which the development of leukemia in the recipient rats was prevented by incubating the cells, prior to injection, with a monoclonal antibody W3/25-ricin conjugate that was selectively toxic to the leukemic cells is described. The W3/25 ricin conjugate was extremely effective in inhibiting protein synthesis by PVG leukemic cells. Leucine uptake was reduced by 50% on treatment of the cells for 1 hr at 37 C with the conjugate at a concentration of 1.4 nanog/ml ricin (2.2 x 10(-11) M). The percentage of cells which survived treatment with the conjugate in vitro was estimated by comparing the time that elapsed between the injection of the treated cells into PVG recipients and the appearance of leukemic cells in the peripheral blood with that observed when graded doses of untreated leukemic cells were injected. Rats which received 10(7) leukemic cells treated with the conjugate at 2.1 ug/ml ricin (10 ug/ml IgG) for 1 hr at 37 C in 100 milliM lactose and then washed twice in lactose-containing medium developed leukemia 8-10 days later than the recipients of untreated cells, indicating that the conjugate had destroyed approx 99.9% of the leukemic cells. Neither the treatment of cells in the presence of lactose with W3/25 antibody alone at 20 ug/ml nor treatment with antibody MRC OX8-ricin at 4.3 ug/ml ricin delayed the appearance of leukemia in the recipients. All recipients of untreated bone marrow/leukemic cell mixtures developed leukemia before their level of B-cell chimerism had been measured. None of the rats given W3/25-ricin-treated cell mixtures containing 10(3) leukemic cells developed disease and of three recipients of inocula containing 10(4) leukemic cells only developed disease. (14 Refs)

43. T-CELL SUBPOPULATIONS IDENTIFIED BY MONOCLONAL ANTIBODIES AFTER HUMAN MARROW TRANSPLANTATION. I. HELPER-INDUCER AND CYTOTOXIC-SUPPRESSOR SUBSETS.

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Blood; 59(6):1292-1298 1982

Peripheral blood helper-inducer and cytotoxic-suppressor T-cell subpopulations in patients receiving marrow transplants for the treatment of acute leukemia or severe aplastic anemia were quantitated on the fluorescence-activated cell sorter (FACS) using the monoclonal antibodies OKT4 and OKT8, respectively. The relative (percent) and absolute number of OKT4+ cells were severely and persistently depleted for up to 2.7 yr posttransplant. In contrast, the percent and absolute number of OKT8+ cells began to recover within the first 60 days of transplant and subsequently remained at normal or high levels for periods of up to 7.3 yr. There was no significant difference in percent or absolute numbers of OKT8+ cells for patients with or without acute graft-vs-host disease (GVHD). The reversal of the normal OKT4:OKT8 ratio (2:1) occurred regardless of whether the recipient was given an allogeneic, syngeneic, or autologous transplant and regardless of whether or not acute or chronic GVHD developed. The reversed ratio was due in the first 3 mo posttransplant to low numbers of OKT4+ cells and later to a combination of low numbers of OKT4+ and high numbers of OKT8+ cells. Normalization and then an increase in the number of OKT8+ cells correlated with increasing time posttransplant and not with resolution of acute GVHD. (Author abstract) (21 Refs)

44. A MONOCLONAL ANTIBODY WITH ANTI-BURKITT LYMPHOMA SPECIFICITY. I. ANALYSIS OF HUMAN HAEMATOPOIETIC AND LYMPHOID CELL LINES.

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Int J Cancer; 29(6):653-658 1982

There is a hybridoma-produced monoclonal rat IgM (38-13) which appears to define a Burkitt's lymphoma-associated antigen (BLA). In this paper, we describe the reactivity of 38-13 with a panel of human hematopoietic and lymphoid cell lines. In indirect immunofluorescence (IF) assays, 15 of 26 Burkitt's lymphoma (BL) lines studied were clearly stained with 38-13 (from 13 to 100% positive cells) by microscope, with varying numbers of heavily labeled cells. In these positive cell lines, fluorescence-activated cell-sorter (FACS) analysis demonstrated that BLA was actually present on all the cells. Positive BL included Epstein-Barr virus (EBV) genome-carrying lines and EBV-negative ones; thus, BLA is not related to the presence of EBV. Most of the 15 BL cells that reacted with 38-13 contained a typical t(8;14) translocation, but had variant translocations such as t(2;8) and t(8;22). The cells were derived from BL patients of different geographical origins and clinical features. Four BL lines were poorly stained and seven were negative with 38-13 in IF assays. The 32 EBV-positive lymphoblastoid cell-lines (LCL) studied were negative. In three line pairs, consisting of a tumor line and an LCL from the same patient, only the BL line was demonstrated to react with 38-13. A series of non-BL cells, including hematopoietic, lymphoid and solid tumor lines, all failed to react with 38-13. Various attempts to modulate the expression of BLA on BL cells were unsuccessful. However, it cannot be ruled out that BLA is actually a transient B-cell differentiation marker. (Author abstract) (18 Refs)

45. ANTIBODIES AND CANCER THERAPY.

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Nature; 297(5865):358-359 1982

The efficacy and safety of using monoclonal antibodies (MA) in cancer therapy are discussed. Problems of MA cross reactivity and antibody specificity are considered. While antibodies to differentiation antigens can be used for tumor therapy, their potential would be greater if tumor-specific antibodies were available. In vitro and in vivo test results for the effects of MA on cancer cells are discussed. (11 Refs)

46. IN VIVO THERAPY OF A MURINE B CELL TUMOR (BCL1) USING ANTIBODY-RICIN A CHAIN IMMUNOTOXINS.

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J Exp Med; 155(6):1797-1809 1982

The therapeutic potential of immunotoxins against the BCL1 mouse tumor model was investigated. Therapy was begun 6-8 wk following inoculation of BALB/c mice with BCL1 cells, at which time animals contained 1-2 x 10(9) tumor cells in spleens, 2-4 x 10(8) tumor cells/ml blood, and 1 x 10(9) tumor cells in liver. After 8-10 fractionated doses of 200 rad total lymphoid irradiation, the number of tumor cells in both spleen and blood of tumor-bearing mice was reduced by 90-95%. Without further treatment, the levels of idiotype (Id) positive cells in the spleen began to rise within a wk and reached 50-80% of pretreatment levels 1-2 wk after termination of radiotherapy. One of two types of immunotoxin were injected into newly irradiated animals. The first was a rabbit anti-Id immunotoxin specific for BCL1 tumor cells. The second immunotoxin was a rabbit anti-delta that was not specific for tumor cells. Administration of either of these immunotoxins caused a measurable delay in the reappearance of tumor cells in the spleens of treated mice. Relapse had occurred by 4 wk, however. Treatment with rabbit anti-delta plus splenectomy resulted in no reemergence of tumor cells for up to 14 wk following irradiation. Sufficient nonspecific cytoreduction of tumor mass before immunotoxin administration was found to be critical. (46 Refs)

47. DISTRIBUTION OF INTERCELLULAR, INTRACYTOPLASMIC AND SURFACE IMMUNOGLOBULINS IN TYPE B NON-HODGKIN'S LYMPHOMA: EMPLOYMENT OF INDIRECT IMMUNOFLUORESCENCE IN THE DETECTION OF IMMUNOMORPHOLOGICAL FEATURES.

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Pathologica; 74(1[illegible]33-45 1982

Immunomorphological patterns of the distribution of surface (SIg) and intracytoplasmic (CIg) immunoglobulins ano free intercellular immunoglobulins (Ig) were examined by immunofluorescence (IF) techniques in 43 patients with type B non-Hodgkin's lymphomas and in 19 patients with reactive hyperplasias. In reactive hyperplasia, primary follicles displayed only SIg-positive cells arranged in a 'honeycomb' pattern; secondary follicles were observed in three concentric areas. In lymphocytic lymphoma (4 cases), the honeycomb pattern was usually observed; the pattern was evenly distributed on the node surface. Very few cells displayed cytoplasmic positivity. Immunocytomas (5 cases) showed diffuse, variously intense SIg-positivity; numerous CIg-positive cells were scattered throughout the preparation. Diffuse centrocytic, centroblastic/centrocytic, and centroblastic lymphomas displayed alternate honeycomb and reticulum areas, interspersed with completely negative areas. Few CIg-positive cells were observed. Monoclonality was seen in two cases. Follicular forms observed in 16 cases of centroblastic/centrocytic lymphoma were usually IF-negative. Very weak honeycombs were detected. Some av size CIg-positive cells were noted in six cases. Completely negative areas interspersed with fields of limited size that displayed weak reticulum or honeycomb positivity in lymphoblastic lymphomas (4 cases). CIg-positive cells were uniformly distributed with monoclonality in two cases. Characteristics of immunoblastic lymphoma (2 cases) were attributable to CIg-positive cells. Probable monoclonality was observed in two cases. (26 Refs)

48. NATURALLY OCCURRING ANTIBODIES AGAINST NINE COMMON ANTIGENS IN HUMANS SERA: II. HIGH INCIDENCE OF MONOCLONAL IG EXHIBITING ANTIBODY ACTIVITY AGAINST ACTIN AND TUBULIN AND SHARING ANTIBODY SPECIFICITIES WITH NATURAL ANTIBODIES.

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J Immunol; 128(6):2788-2792 1982

Previous results prompted us to check the sera of patients carrying either a multiple myeloma or a Waldenstrom's macroglobulinemia for the presence of monoclonal Ig (MIg) having antibody activity against tubulin, actin, thyroglobulin, myoglobin, fetuin, albumin, and transferrin. Among the 62 MIg studied against the seven above-mentioned antigens, 1 was shown to bind extensively to tubulin, and 4 bound mainly to actin, but a significant binding was also found to occur with tubulin and thyroglobulin. In all cases, findings were as follows: (1) The binding was mediated by light and heavy chain isotypes corresponding to those of the MIg. (2) The antibody function was located in the Fab fragments prepared by pepsin digestion of these MIg. (3) The antibody function was inhibited by the antigens. MIg with anti-tubulin activity was exclusively inhibited by tubulin, whereas the four MIg binding mainly to actin were predominantly inhibited by actin, but they were also strongly inhibited by tubulin and thyroglobulin. Similar results were obtained with either the serum or the F(ab')2 fragments. (4) The Fab fragments were tested for their capacity to stain, by immunocytologic procedures, cultured human hepatic cells previously treated with vinblastine. In the case of the serum exhibiting anti-tubulin activity, only paracrystals of tubulin were stained, whereas for the four MIg exhibiting anti-actin activity, simultaneous staining of actin filaments and tubulin paracrystals was observed. Three main conclusions emerge: (1) There is a high incidence of MIg possessing antibody activity directed against the cytoskeleton proteins. (2) These MIg seem to share antibody specificities with natural antibodies. (3) In the latter case, it can be postulated that, at least for some patients, the MIg may constitute the expansion of a clone producing a natural antibody. (14 Refs)

49. HETEROGENEITY OF THE NATURAL HUMORAL ANTI-TUMOR IMMUNE RESPONSE IN MICE AS SHOWN BY MONOCLONAL ANTIBODIES.

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J Immunol; 128(6):2757-2762 1982

Four anti-tumor cytotoxic antibodies, namely, A6 of the IgG2 class and B3, C2, and D1 of the IgM class, were obtained in monoclonal form from hybridization of mouse myeloma cells with spleen cells of normal untreated mice selected for high natural anti-tumor immune responses. The specificity of the four monoclonals was tested by complement-dependent cytotoxicity assay on the reference EL4 lymphoma at different days of in vivo transplant, on normal adult and fetal tissues, on the SC-1 fibroblastic cell line uninfected or infected with a murine ecotropic Type-C virus, and on a panel of murine lymphomas of different origin. The four antibodies had different specificities: the A6 and B3 recognized virus-related structures, the C2 a structure expressed on fetal cells, and the D1 a normal component of fibroblasts. The different classes and specificities of the four monoclonals, as well as their in vitro-demonstrated synergistic cooperation, give support to the hypothesis that the natural humoral anti-tumor cytotoxic immune response could be the result of the cooperative activity of an array of heterogeneous antibody molecules. (Author abstract) (20 Refs)

50. PHENOTYPIC HETEROGENEITY OF HUMAN T-CELL MALIGNANCIES: DEMONSTRATION BY MONOCLONAL ANTIBODIES AND CYTOCHEMICAL MARXERS.

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Am J Hematol; 12(3):233-245 1982

The present study sought to delineate the phenotypic heterogeneity of the human T-cell malignancies. Twenty T-cell neoplasms were investigated for reactivity with the OKT hybridoma monoclonal antibodies and expression of acid alpha-naphthyl acetate esterase (ANAE), beta-glucuronidase (BG), and acid phosphatase (AP) activity. Twelve cases (Mycosis fungoides, Sezary syndrome, cutaneous T-cell lymphoma, chronic lymphocytic leukemia) were OKT3+T4+, ie, expressed the phenotype commonly associated with mature T-helper cells. These cases were further divisible into ANAE+BG+ (6 cases), ANAE-BG+ (5 cases), and ANAE-BG- (1 case) phenotypes. In contrast to the 12 OKT3+T4+ cases, the remaining 8 cases showed considerable inter- and intratumor heterogeneity with respect to reactivity with the OKT antibodies. Six of these cases (acute lymphoblastic leukemia, lymphoblastic lymphoma) expressed phenotypes consistent with various intrathymic stages of T-cell differentiation. Five of the latter six cases were AP+BG+ANAE-, analogous to the majority of normal cortical thymocytes; an OKT3+T4-T8+T10+ neoplasm was ANAE+, analogous to normal medullary thymocytes. Two cases expressed the previously undescribed OKT3+T4-T8-T10+ phenotype. These studies demonstrate that the T-cell malignancies are divisible into phenotypes which correspond to normal maturational stages of T-cell differentiation and functionally distinct T-cell subsets. Phenotypic analysis of the human T-cell malignancies may provide a basis for understanding their biological heterogeneity and may aid in the identification of transitional stages of T-cell differentiation and minor T-cell subsets. (Author abstract) (21 Refs)

51. IMMUNE-MEDIATED PLATELET DESTRUCTION AND THROMBOCYTOPENIA IN PATIENTS WITH SOLID TUMOURS.

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Br J Haematol; 51(1):17-24 1982

Autoimmune mediated platelet destruction with severe thrombocytopenia was documented in eight patients with solid tumors. The patients had reduced platelet lifespan, a positive platelet antibody tests, increased numbers of megakaryocytes, and arise in platelet count following treatment with steroids, splenectomy or immunosuppressive therapy. Intravascular coagulation was excluded as the predominant cause of thrombocytopenia by near normal 125I-fibrinogen survival; thrombocytopenia secondary to marrow suppression was ruled out by increased platelet turnover. Thus, like patients with lymphoproliferative disorders, patients with solid tumors may be thrombocytopenic because of immune mediated platelet destruction. (Author abstract) (19 Refs)

52. CHANGES IN SUSCEPTIBILITY TO CYTOTOXIC ANTIBODY AMONG TUMOR CELLS SURVIVING EXPOSURE TO CHEMOTHERAPEUTIC AGENTS.

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Cancer Res; 42(7):2622-2627 1982

We determined that myeloma cells which survived drug treatment had an altered sensitivity to cytotoxic antibody. The effects of several chemotherapeutic agents differing in drug action was compared. The antiserum was directed against viral determinants on the surface of S107 myeloma cells. This antiserum was then used to inhibit the colony formation of drug-treated myeloma cells. Tumor cells were treated with melphalan (200 ng/ml), methotrexate (40 ng/ml), actinomycin D (5 ng/ml), or 0.5 mM thymidine for 24 hr and then washed and resuspended in fresh medium. On various days after drug treatment, aliquots of these cells were exposed to complement and dilutions of antiserum and then cloned in soft agar in order to quantify the degree of antibody-mediated inhibition. Melphalan, methotrexate, and thymidine caused a severalfold increased resistance of the tumor cells to the antiserum during the first 1 or 2 days after drug treatment. During the following days, however, myeloma cells showed markedly increased susceptibility to the antiserum. The biphasic effects of methotrexate or thymidine treatment was similar to that previously observed after melphalan treatment and differed from the effect of actinomycin D. Actinomycin D caused only an increased susceptibility of the tumor cells to the antibody for a period of 4 to 5 days immediately following drug treatment. Our studies indicate that several chemotherapeutic drugs at concentrations comparable to those used in humans have long-lasting antagonistic as well as synergistic effects on the sensitivity of tumor cells to antibody and complement, depending on the particular drug used and on the time interval between drug exposure and subsequent treatment with antibody. These results suggest a model for evaluating the use of antibody in the elimination of malignant cells which, despite exposure to chemotherapy, remain clonogenic and proliferative. (Author abstract) (18 Refs)

IMMUNOGLOBULIN STRUCTURE AND SYNTHESIS

53. A HUMAN MYELOMA CELL LINE THAT DOES NOT EXPRESS IMMUNOGLOBULIN BUT YIELDS A HIGH FREQUENCY OF ANTIBODY-SECRETING HYBRIDOMAS.

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J Immunol; 129(1):406-412 1982

We selected an 8-azaguanine-resistant variant of a human myeloma cell line (RPMI 8226) by cloning the parental cells on a feeder layer of mouse spleen cells in the presence of increasing concentrations of 8-azaguenine. Culture media and cellfree extracts of both the parental and variant (8226 AR/NIP4-1) cell lines were assayed for production of immunoglobulin heavy and light chains by double immunodiffusion and for lambda-chain by radioimmunoassay. Secretion of free lambda-chain by the parental cell line was confirmed. In contrast, no immunoglobulin heavy or light chains were detected in culture medium of the variant cell line by either immunodiffusion or radioimmunoassay. No intracellular lambda-chain could be detected in the variant cells by radioimmunoassay of cellfree extracts or by immunofluorescence of fixed cells. Hybridomas were produced by fusion of 8226AR/NIP4-1 cells with lymphocytes from a mesenteric lymph node recovered at surgery from a hypertransfused renal transplant recipient. Twenty hybrid culture supernatants were assayed for immunoglobulin by double immunodiffusion, and 15 contained either IgG (lambda) or IgG (kappa). None produced IgM or IgA. An IgG (kappa)-producing hybridoma was shown by immunofluorescence not to express lambda-chain. A second fusion between the variant cell line and spleen cells from a renal transplant patient produced a stable hybridoma secreting IgM (lambda) antibody specific for the I antigen. (Author abstract) (30 Refs)

54. ARRANGEMENT OF LAMBDA LIGHT CHAIN GENES IN MUTANT CLONES OF THE MOPC 315 MOUSE MYELOMA CELLS.

Hozumi N, Wu G, Murialdo H, Baumal R, Mosmann T, Winberry L, Marks A
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J Immunol; 129(1):260-266 1982

The synthesis of lambda light chains and the arrangement of the lambda-chain genes was examined in cells of the mouse myeloma MOPC 315, which is an alpha lambda2 producer, and in several mutants derived from it. The mutants produce lambda2 chains only (MOPC 315.26, MOPC 315.34, and MOPC 315.37) or fail to produce alpha and lambda2 chains (MOPC 315.35 and MOPC 315.36). Messenger RNA from lambda2 chain-producing cells directed the synthesis of a lambda2 chain precursor and a fragment of the lambda1 chain (lambda1F) in a wheat embryo cell free system, whereas mRNA from the cells that do not produce lambda2 chains directed the synthesis of lambda1F only. DNA from the parental MOPC 315 cells and from the lambda2 chain-producing cells contained discrete EcoRI restriction fragments coding for rearranged lambda1 and lambda2 chain genes and their respective germ-line V and J-C regions. DNA from the non-Ig-producing cells contained fragments coding for the rearranged lambda1 chain gene and the germ-line Vlambda2 region, but it lacked the sequences coding for the rearranged lambda2 chain gene and the germ-line Vlambda1 and J-Clambda1 regions. These results suggest that rearrangements of the lambda1 and lambda2 chain genes occur on different chromosomes in MOPC 315 cells and imply that rearrangements of the lambda1 and lambda2 chain genes on the same chromosome may be mutually exclusive. (Author abstract) (37 Refs)

55. PHYSICOCHEMICAL AND IMMUNOCHEMICAL CHARACTERISTICS OF HEAVY CHAINS OF CANCER-SPECIFIC IGG.

Sen'ko LN, Protsenko BA, Korotkoruchko VP
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Ukr Biokhim Zh; 54(3):243-248 1982

Results of physicochemical and immunochemical analysis of IgG isolated from sera of myeloma G patients are reported. Thin layer gel filtration showed significant decreases in mol wt of heavy chains of cancer-specific IgG (43,000 daltons, compared with 49,500-51,000 daltons for IgG of healthy controls). The decrease in mol wt was associated with a significant decrease in number of amino acid residues. Double immunodiffusion technique showed that rabbit antiserum to the cancer-specific IgG precipitated gamma chains of the cancer-specific IgG but not gamma chains of IgG from healthy controls. These findings indicated that heavy chains of cancer-specific IgG contained antigenic determinants. Analysis of cyanogen bromide fragments showed changes in content of tripeptides. It was concluded that the differences in the physicochemical properties of the cancer-specific IgG are associated with changes in primary structure. (29 Refs) (In RUS)

56. IMMUNOGLOBULIN PRODUCTION AFTER MARROW TRANSPLANTATION. III. THE FUNCTIONAL HETEROGENEITY OF FC-IGG RECEPTOR POSITIVE AND NEGATIVE T CELL SUBPOPULATIONS.

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Clin Exp Immunol; 48(3):675-684 1982

Ten patients with chronic graft-vs-host disease (GVHD) after HLA-identical marrow transplantation were studied between 372 and 1,649 days post-transplant for their T cell subset functions in pokeweed mitogen-stimulated immunoglobulin (Ig) synthesis. In vitro Ig synthesis was assessed using an indirect hemolytic plaque assay after 6 days of culture. T cells, TG+ cells (Fc-IgG receptor positive), TG- cells (Fc-IgG receptor negative), and B cell-enriched populations from the patients were co-cultured with normal T and/or B cells. Such cultures in patients with chronic GVHD showed deficient B cell activity (8 of 10); and deficient helper activity in T cells (6 of 10), TG+ cells (5 of 9), and TG- cells (3 of 9). Greater than 50% suppression of Ig synthesis was detected with T cells (4 of 10), TG+ cells (3 of 10), and TG- cells (3 of 10). This study provides evidence for variable regulatory function of Fc receptor T cell subsets in patients with chronic GVHD. The unexpected finding was that TG+ and TG- subpopulations can lack helper activity or actively suppress Ig synthesis. (Author abstract) (32 Refs)

57. MONOCLONAL IMMUNOGLOBULIN-SECRETING LYMPHOMA IN A PATIENT WITH SEVERE COMBINED IMMUNODEFICIENCY DISEASE.

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Clin Exp Immunol; 48(3):666-674 1982

A 3.5 yr old boy with X-linked severe combined immunodeficiency disease (SCID), who had been in laminar flow isolation throughout his life, developed a B cell tumor producing up to 3,008 mg/dl of the IgM kappa paraprotein 1 mo after infusion of both liver and thymus cells from a fetal donor and 6 mo after the last of six fetal liver cell infusions given over a 3 yr period. Pretransplant studies revealed a high percentage of circulating B lymphocytes. HLA typing suggests that the tumor was of host origin. (Author abstract) (20 Refs)

58. NATURAL AND ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY IN TUMOR-ADHERENT T LYMPHOCYTES: EXPRESSION OF FC RECEPTORS AND OF A HUMAN T-SUBGROUP-SPECIFIC ANTIGEN.

Feucht HE, Hadam MR, Lohmeyer J, Frank F, Rieber EP, Riethmuller G
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Scand J Immunol; 15(5):483-492 1982

Adherence of human lymphocytes to allogeneic tumor cell monolayers was found to depend on the presence of monocytes. Adherent lymphocytes could be separated from tumor cells by treatment with lidocaine followed by nylon wool passage. Tumor-adherent cells (70% E-RFC, 45% Fcgamma-R, 23% Fcu-R, 5% monocytes) exhibited enriched natural killer (NK) activity not only against the tumor cell line used for isolation but also against seven other targets. When T cells were isolated subsequently as E-rosettes by density gradient centrifugation through Percoll, the enrichment in cytotoxicity was even more pronounced. Tumor-adherent T cells were several-fold enriched in both NK and antibody-dependent cell-mediated cytotoxicity (ADCC) activity. However, this enrichment was not paralleled by a concomitant increase in the number of Tgamma cells (tumor-adherent T cells: 17% Tgamma, 40% Tmu; tumor-nonadherent T cells: 12% Tgamma, 60% Tmu). Marked differences could be observed by staining with a monoclonal antibody that was raised against human leukemic Tgamma cells of high NK and ADCC activity. This antibody (T 8-11) stained 60% of tumor-adherent T cells, 20% of nonadherent T cells and 29% of T-cell controls. These results indicate that the spontaneous cytotoxic activity of human T cells resides within a small population, most of which are characterized by a specific surface antigen but not by conventional Fcgamma receptors. (Author abstract) (41 Refs)

59. RELATIONSHIP BETWEEN THE REARRANGEMENT OF IMMUNOGLOBULIN GENES, THE APPEARANCE OF A B LYMPHOCYTE ANTIGEN, AND IMMUNOGLOBULIN SYNTHESIS IN MURINE PRE-B CELL LINES.

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J Immunol; 128(6):2793-2797 1982

Eighteen Abelson virus-transformed immature B cell lines were established and immunoglobulin biosynthesis, expression of a B lymphocyte antigen detected by a monoclonal antibody, and rearrangement of immunoglobulin genes in these cell lines were studied. Only one cell line (A1) synthesized mu-chains but no light chains, and the other cell lines synthesized no detectable immunoglobulins. None of the cell lines established had detectable membrane-associated IgM. Fifteen cell lines expressed a B lymphocyte antigen on their cell surfaces. In three cell lines, however, the majority (greater than 99%) of cells did not express this antigen. Heavy chain genes were rearranged on both chromosomes in all the cell lines, although one heavy chain gene was deleted in three cell lines. In 12 of 18 cell lines, one or both kappa-chain genes were rearranged. In six cell lines, however, both kappa-chain genes remained in embryonic form; lambda-chain genes were in embryonic form in all the cell lines. These results suggested the hierarchy of Ig gene rearrangements, beginning with mu and proceeding to kappa and then to lambda. JH rearrangement was also shown to precede the appearance of a B lymphocyte antigen. In three cell lines (A1-A3), which were considered subclones derived from a single common precursor, it was suggested that one rearranged JH gene was functional, and the other was nonfunctional, indicating that allelic exclusion already operated in pre-B cells. (Author abstract) (23 Refs)

60. ASYMMETRICAL SURFACE IGG ON MOPC-21 PLASMACYTOMA CELLS CONTAINS ONE MEMBRANE HEAVY CHAIN AND ONE SECRETORY HEAVY CHAIN.

Goding JW
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J Immunol; 128(6):2416-2421 1982

Membrane proteins from the B lymphomas WEHI-231 and 2PK3 and from the plasmacytomas MPC-11 and MOPC-21 were radioiodinated in situ by the lactoperoxidase method and were subjected to two-dimensional (nonreduced, reduced) polyacrylamide gel electrophoresis in the presence of sodium dodecyl sulfate. Few heavily labeled membrane proteins were composed of disulfide-bonded subunits. One such protein (mw 200,000 intact and 116,000 reduced) shared some properties with the PC-1 alloantigen, although it was not conclusively identified. A second major disulfide-bonded protein (mw 200,000 intact and 95,000 reduced) has been identified previously as the receptor for transferrin. Membrane immunoglobulins of WEHI-231 (IgM) and 2PK3 (IgG2a) had the expected subunit structure, whereas membrane immunoglobulin was not detected on MPC-11. In contrast, surface IgG1 of MOPC-21 appeared to consist almost entirely of hybrid molecules containing one membrane gamma1 chain and one secretory gamma1 chain. This hybrid IgG molecule appeared to exist in both monomeric and dimeric forms. It is concluded that (i) the synthetic and assembly mechanisms of secretory and membrane IgG1 are shared; (ii) there are no special mechanisms to prevent pairing of membrane and secretory gamma1 chains; (iii) the presence of one hydrophobic tail is sufficient for membrane insertion of gamma1 chains; and (iv) the C-terminal extension cysteine residues of membrane gamma1 chains in hybrid IgG molecules are either unpaired or may allow the formation of hybrid IgG dimers. (Author abstract) (37 Refs)

61. IMMUNOPEROXIDASE CHARACTERIZATION OF A PHARYNGEAL PLASMACYTOMA.

Humphrey DM, Aufdemorte TB, Mattox DE
Dept. Pathology, Univ. Texas Health Science Center, 7703 Floyd Curl Dr., San Antonio, TX, 78284
Arch Otolaryngol; 108(6):362-365 1982

Extramedullary plasmacytomas (EMPs) are plasma cell neoplasms that most frequently arise along the upper airways and often do not secrete detectable amounts of M protein at the time of diagnosis. The present report describes the immunohistochemical characterization of an EMP in a young woman. The unlabeled peroxidase-antiperoxidase method was employed to demonstrate cytoplasmic immunoglobulin determinants in routinely processed, paraffin-embedded tissue. Only kappa light chain and gamma heavy chain determinants were found in the cytoplasm of the neoplastic plasma cells; essentially identical results were found in both initial and recurrent lesions separated by a 16-mo interval. This exclusive staining of one light chain type associated with only one heavy chain represents a monoclonal staining pattern that is typical of B-cell neoplasms. Such characterization of EMPs on the basis of cytoplasmic immunoglobulin class and type may provide prognostic information analogous to the classification of multiple myeloma by immunoelectrophoresis. (Author abstract) (28 Refs)

62. LOSS OF SURFACE-BOUND ANTIBODY ACCOMPANYING THE ANTI-COMPLEMENTARY MODULATION OF LEUKEMIC B CELL IMMUNOGLOBULIN: CONTRASTING EFFECTS OF ANTIBODIES DIRECTED AGAINST IDIOTYPIC AND CONSTANT REGIONS.

Gordon J, Anderson VA, Stevenson GT

Dept. Tumor Biology, Karolinska Inst., Box 60400, S-104 01 Stockholm, Sweden

J Immunol; 128(6):2763-2769 1982

Guinea pig L2C leukemia lymphocytes display at their surfaces monoclonal IgM, which when complexed with antibody undergoes rapid redistribution and variable endocytosis. One consequence of this is that the cells can prove resistant to lysis by complement subsequently added to the system, a process termed here anti-complementary modulation. We studied quantitatively the extent of antibody loss accompanying the modulation by radioimmunolabeling the cell surfaces with 125I-Fab'-gamma fragments from an anti-antibody. Antibody directed against the constant region of the IgM light chain (anti-lambda) gave modulation effective against syngeneic (guinea pig strain 2) complement that closely paralleled the disappearance of anti-lambda from the cell surfaces. Antibody directed against the idiotypic region of the light chain (anti-Id) was as effective as anti-lambda in modulating against syngeneic complement. However, the bulk of the anti-Id was seen by radioimmunolabeling to persist on the surfaces of the resistant cells, even after prolonged exposure at 37 C, and was shown by immunofluorescence to be in a patched configuration. In contrast to the results with syngeneic complement, modulation effective against rabbit complement appeared to have an absolute requirement for clearing of the antibody: thus anti-lambda could modulate, anti-Id could not. The differences observed between anti-lambda and anti-Id could not be accounted for by differences in their isotypic (Ig subclass) composition nor by the numbers of antibody molecules bound. Studies with directly fluoresceinated and 125I-labeled and anti-lambda revealed endocytosis rather than shedding was the major route of antibody loss from the cell surfaces over the period of anti-complementary modulation. The findings are discussed in relation to mechanisms that enable leukemic B lymphocytes to escape destruction when confronted by antibody and complement. (Author abstract) (32 Refs)

HUMORAL IMMUNE BLOCKING FACTORS AND ANTIGEN-ANTIBODY COMPLEXES

63. LEVELS OF CIRCULATING IMMUNE COMPLEXES IN PATIENTS WITH OVARIAN CANCER.

Clarke AG, Vasey DP, Symonds EM, Faratian B, McLaughlin PJ, Price MR, Baldwin RW
Dept. Obstetrics and Gynecology, Univ. Hosp., Queen's Medical Centre, Nottingham NG7 2UH, England
Br J Obstet Gynaecol; 89(3):231-237 1982

Sera from patients with ovarian tumors were assayed for circulating immune complexes (CIC) by four well established assays based on the interaction of immune complexes with components of the complement system. There was no difference in control, pre- or post-operative or BCG-treated patients' sera. Levels were also unchanged in sera in antigen excess. In patients with ovarian tumors before the measurement of CIC would appear to be of little value as a screening test, as a guide to the extent of disease, prognosis or therapy. In a small pilot therapy-trial there was no difference in the survival rate between patients with Stage III and IV ovarian cancer treated with cyclophosphamide plus BCG and those who received only cyclophosphamide. Treatment with BCG was associated with postoperative pyrexia and a prolonged hospital stay. (Author abstract) (43 Refs)

64. HETEROGENEITY OF CIRCULATING IMMUNE COMPLEXES IN LUNG CANCER AND OTHER CHRONIC PULMONARY DISEASES (MEETING ABSTRACT)

Cooper KM, Moore M
Christie Hospital and Holt Radium Institute, Manchester, England
Twenty-third Annual General Meeting of the British Association for Cancer Research, March 29-31, 1982, Edinburgh, Scotland. British Association for Cancer Research 78 pp., 1982.

Circulating immune complex (IC) levels in sera from 58 healthy controls and a total of 212 patients with various chronic lung diseases including 74 with bronchial carcinoma were measured using three assays: Two complement-dependent assays (C1q fluid phase and Raji) and a complement-independent assay (L1210). The three assays generally revealed similar patterns of reactivity when control and pathological groups were compared but the L1210 assay invariably demonstrated the lowest incidence of positive values in each group. The most significant elevations in IC levels were exhibited in bronchiectasis (chronic bronchial suppuration) and bronchial carcinoma. However, within these two groups correlations between IC assay performed on individual sera were poor. Significant but weak correlations were only observed for C1q vs Raji in bronchiectasis and Clq vs L1210 in bronchial carcinoma. Complement-binding ICs were present to a similar extent in both conditions. However, non-complement binding ICs were found to be more common in bronchiectasis. (no Refs)

65. REACTIVITY WITH PATIENT ANTIBODIES OF PARTIALLY PURIFIED GP40 ANTIGEN FROM IMMUNE COMPLEXES IN BURKITT'S LYMPHOMA AND NASOPHARYNGEAL CARCINOMA.

Gazitt Y, Klein G, Sulitzeanu D
Lautenberg Center for General and Tumor Immunology, Hebrew Univ. Hadassah Medical Sch., Jerusalem, Israel
Int J Cancer; 29(6):645-651 1982

A glycoprotein antigen (gp40) was previously identified as a major component of immune complexes isolated from sera of patients with Burkitt's lymphoma (BL) and nasopharyngeal carcinoma (NPC). In the present work gp40 was partially purified from a pool of BL/NPC sera. Sera of patients with BL and NPC as well as sera of patients with other malignant and non-malignant diseases were tested for antibodies against gp40, using a double antibody radioimmunoassay. Practically all normal sera and sera of patients with non-malignant diseases had antibodies capable of binding radioiodinated gp40. In contrast, sera of patients with BL or NPC had very low binding, while sera of patients with other malignant diseases had intermediate binding values. The low binding activity of BL/NPC sera was shown to be due to inhibition by excess gp40 present in such sera. Effusions of patients with breast or ovarian cancer also contained demonstrable amounts of gp40. The origin of gp40 is still unknown. (Author abstract) (25 Refs)

66. GLOMERULAR IMMUNE COMPLEX FORMATION AND INDUCTION OF LYMPHOMA IN ATHYMIC NUDE MICE BY TISSUE FILTRATES OF CROHN'S DISEASE PATIENTS.

Williams SE, Valenzuela I, Kadish AS, Das KM
(c/o Das) Div. Gastrointestinal and Liver Disease, Albert Einstein Coll. Medicine, 1300 Morris Park Ave., Bronx, NY, 10461
J Lab Clin Med; 99(6):827-837 1982

Lymph nodes and intestinal filtrates from Crohn's disease patients produced lymphoma in 5 and plasma cell hyperplasia in 2 of 63 athymic (nu/nu) mice. None of 27 mice injected with intestinal filtrates from ulcerative colitis patients but one of 13 mice injected with normal-appearing colon developed lymphoma. With an indirect immunofluorescence technique, sera from all 9 patients with symptomatic Crohn's disease and 1 of 15 patients with asymptomatic Crohn's disease demonstrated cytoplasmic immunofluorescence in a lymphoma produced by Crohn's disease filtrates, but not in a control filtrate-induced lymphoma. None of 46 sera from ulcerative colitis patients or control subjects demonstrated immunofluorescence. In addition, immunofluorescent staining with symptomatic Crohn's disease sera recognized an antigen(s) within glomeruli that were also stained with anti-mouse IgG and IgM. Kidneys from the control mice did not show any staining. These studies suggest that an agent present in lymph nodes and intestine of patients with Crohn's disease can induce lymphoma and glomerular immune complexes in nu/nu mice. (Author abstract) (27 Refs)

67. TWO-DIMENSIONAL GEL ELECTROPHORESIS OF MEMBRANE PROTEINS FROM THE R3327 PROSTATE ADENOCARCINOMA.

Kozlovskis PL, Claflin AJ, Fletcher MA, McKinney EC, Rubin RW
Dept. Medicine (D-39), Univ. Miami Sch. Medicine, P.O. Box 016960, Miami, FL, 33101
Cancer Res; 42(7):2748-2756 1982

The Dunning rat prostate adenocarcinoma (R3327) is a reliable model that shares many similarities with the human tumor. Two sublines of the tumor, G and H, represent opposite extremes in histology and growth rate. Purified membrane fractions from G and H solid tumors were isolated by sucrose gradient. Tumor and normal prostate membrane proteins were labeled with 125I, incubated with G or H antisera, and precipitated by absorption of antibody-antigen complexes to staphylococcal Protein A. Proteins were resolubilized and electrophoresed on two-dimensional gels, and the gels were autoradiographed. A total of eight labeled proteins were precipitated from the G and H tumors in the presence of G antisera. Of these, seven were homologous. One high-mol-wt protein (Protein b) present on the G tumor was absent from the H tumor. The H tumor contained high-mol-wt protein (i) that was not found on the G tumor or on normal prostate. Normal prostate revealed a pattern similar to the G tumor except that Protein b appeared to be quantitatively reduced. Precipitation in the presence of H antisera showed similar patterns except that Protein b was not detected in the G tumor and was greatly reduced in the normal prostate. Therefore, despite variable growth characteristics, there were few changes in membrane proteins between the solid tumors and between the tumors and normal prostate. Iodination of surface proteins of cultured cells from normal prostate and the G and H sublines also showed a high degree of homology. No consistent differences between cultured cell lines were noted. (Author abstract) (27 Refs)

68. ISOLATION AND CHARACTERIZATION OF CIRCULATING FELINE LEUKEMIA VIRUS-IMMUNE COMPLEXES FROM PLASMA OF PERSISTENTLY INFECTED PET CATS REMOVED BY EX VIVO IMMUNOSORPTION.

Snyder HW, Jones FR, Day NK, Hardy WD
Lab. Viral Oncology, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
J Immunol; 128(6):2726-2730 1982

IgG and circulating IgG immune complexes (CIC) were purified from plasma of three pet cats persistently infected with feline leukemia virus (FeLV) by adsorption to, and elution from, Staphylococcus aureus Cowan I. CIC were then separated from free IgG by sucrose gradient ultracentrifugation and were analyzed for the presence of FeLV structural proteins and corresponding specific antibodies. Radioimmunoprecipitation analysis indicated that FeLV envelope (gp70) and major core (p30) proteins, along with cat IgG heavy and light chains, were present in the CIC from all three cats. Further analysis of the CIC from one of the cats also revealed the presence of FeLV core proteins p15 and p12. IgG purified from isolated CIC was also shown to bind specifically to purified FeLV gp70, p30, and p15. These data provide direct evidence for FeLV-specific CIC in the plasma of persistently viremic pet cats, and suggest these animals are immunologically responsive to the virus even though free antibodies against the major structural proteins cannot be demonstrated in standard assays. (Author abstract) (32 Refs)

HUMORAL IMMUNOSUPPRESSIVE AGENTS

69. SUCCESSFUL TREATMENT OF PULMONARY AND CEREBRAL ASPERGILLOSIS IN AN IMMUNOSUPPRESSED CHILD.

Henze G, Aldenhoff P, Stephani U, Grosse G, Kazner E, Staib F
Kinderklinik und Poliklinik, Freien Universitat Berlin, Heubnerweg 6, D-1000 Berlin, W. Germany
Eur J Pediatr; 138(3):263-265 1982

A 12-yr-old boy with CNS relapse of acute lymphoblastic leukemia developed invasive pulmonary and cerebral aspergillosis during antineoplastic treatment. Pulmonary infiltrates completely regressed after treatment with amphotericin B and 5-fluorocytosine. No viable fungi could be detected in a completely resected cerebral abscess after a 4-wk course of antifungal therapy and neurologic symptoms disappeared. The infectious agent may have come from a potted plant in the patient's house. (10 Refs)

70. INFECTIONS IN IMMUNOSUPPRESSED RECIPIENTS OF BONE MARROW.

Beliakov VA, Liubimova LS, Martynova VA, Ermakova GL, Fainshtein FE
Central Res. Inst. Hematology and Blood Transfusion, Moscow, USSR
Probl Gematol Pereliv Krovi; 27(5):9-11 1982

Incidence and spectrum of infectious complications were studied in 25 patients (14 men, 11 women; 16-49 yr old) who were subjected to transplantation of bone marrow. Among these patients, 11 had hypoplastic anemia, 2 had paroxysmal hemoglobinuria, and 12 had acute leukemia. Prior to transplantation, the patients received immunosuppressive therapy with antilymphocyte globulin (ALG), cyclophosphamide (CP), and whole-body irradiation. Severe infections were observed in 50% of the patients treated with ALG, 50% of those treated with CP alone, and 100% of those treated with CP in combination with whole-body irradiation. (1 Ref) (In RUS)

OTHER RELATED STUDIES

71. DISTINCT SIGNALS FOR ANTIBODY-DEPENDENT AND NONSPECIFIC KILLING OF TUMOR TARGETS MEDIATED BY MACROPHAGES.

Ralph P, Williams N, Nakoinz I, Jackson H, Watson JD
Dept. Developmental Hematopoiesis, Memorial Sloan-Kettering Cancer Center, Rye, NY, 10580
J Immunol; 129(1):427-432 1982

Conditions influencing the generation of antibody-dependent cellular cytotoxicity (ADCC) and several types of nonspecific tumor cell killing by macrophages were compared. Resident mouse peritoneal macrophages and several macrophage cell lines spontaneously display very low levels of ADCC to lymphoma targets. However, ADCC could be greatly stimulated in these macrophage populations by several days of culture with lipopolysaccharide (LPS), tumor promoter phorbol myristic acetate (PMA), and lymphokine (LK) preparations. Fibroblast L cell-conditioned medium (L-CM), a source of activities required for in vitro macrophage colony formation, also augmented ADCC. Two days of preincubation was optimal for stimulation of this cytotoxic activity. In contrast to these results, pretreatment of macrophages with any of the agents inhibitor tumor toxicity induced by nonspecific activating drugs present during the assay. This inverse relation between ADCC and nonspecific killing after pretreatment was obtained with peritoneal cells and two cloned macrophage cell lines. Thus, although the same cell or cell type can mediate both types of killing, the two mechanisms seem to be mediated by distinct states of a macrophage. The ADCC-stimulating agents, LPS, LK, and L-CM, probably have a common pathway of activation, because dexamethasone at 10(-6) M inhibited their effect. The factors in the LK and L-CM that stimulate ADCC are distinct from LPS, because the endogenous activities were inactivated by boiling. The activities are also separate from interleukin 2 and myeloid colony-stimulating factor purified from L-CM, CSF-1, had no effect on macrophage tumoricidal activity. ADCC-stimulating activity was not the same as macrophage-activating factor for nonspecific killing of fibrosarcoma targets, because the latter is not found in L-CM. It is concluded that macrophage ADCC and nonspecific cytotoxicity may be regulated by different endogenous signal and may represent different states of stimulated macrophages. (Author abstract) (41 Refs)

72. PHORBOL ESTER TUMOR PROMOTER MODULATION OF ALLOANTIGEN-SPECIFIC T LYMPHOCYTE RESPONSES.

Andreotti PE
Div. Immunology, Duke Univ. Medical Center, Durham, NC, 27710
J Immunol; 129(1):91-96 1982

The phorbol diester tumor promoter phorbol 12-myristate 13-acetate (PMA) was studied for its effects on T lymphocyte activation in allogeneic human mixed lymphocyte cultures. Lymphocyte proliferation was significantly enhanced in cultures with PMA at concentrations greater than or equal to 12.5 ng/ml, and interferon-gamma production was synergistically increased in cultures with PMA at concentrations greater than or equal to 5 ng/ml. In contrast, the generation of HLA-specific cytotoxic lymphocyte activity was completely inhibited in cultures with PMA at concentrations greater than or equal to 5 ng/ml. Fluorescence-activated cell sorter analysis with OKT mouse monoclonal antibodies indicated these PMA effects on lymphocyte activation are associated with an increase in the number of activated OKT4-positive T lymphocytes. (Author abstract) (41 Refs)

73. DERIVATION OF MACROPHAGE-LIKE LINES FROM THE PRE-B LYMPHOMA ABLS 8.1 USING 5-AZACYTIDINE.

Boyd AW, Schrader JW
Walter and Eliza Hall Inst. Medical Res., Post Office, Royal Melbourne Hosp., Melbourne, Victoria 3050, Australia
Nature; 297(5868):691-693 1982

Cloned ABLS 8.1 cells were cultured in the presence of various concentrations of 5-azacytidine (AC). Cells that survived culture with 1 uM AC were cloned with culture medium containing 2-mercaptoethanol (ME). Seven of 16 cell lines showed characteristics different from the parental line. A second series of variant lines was obtained without the use of ME. Both sets of cell lines have been re-cloned and have remained stable for over 3 mo of continuous culture. The granules and vacuoles present in these cells give them the superficial appearance of macrophages. A number of tests were performed on the derived and parent cells which indicated the derived cells possessed characteristic of macrophage cell lines. The most impressive test was phagocytosis of opsinized RBC which was not seen in control ABLS 8.1 cells and seems to be a unique property of macrophages. Other supporting evidence was the presence of esterase-positive granules and the presence on many of the cells of an antigen detected by the macrophage-specific monoclonal antibody (Mac-1). It is concluded that the demethylating drug AC has induced heritable morphological and functional changes in the pre-B-cell line ABLS 8.1 characterized by expression of macrophage-like features. (24 Refs)

74. MEDIATION OF CELLULAR IMMUNITY IN CANCER BY IMMUNE MODIFIERS.

Chirigos MA, Mastrangelo MJ, Mitchell M, Krim M
Viruses and Disease Modification Section, Div. Cancer Treatment, NCI, NIH, Bethesda, MD, 20205
Prog Cancer Res Ther; 190:1-275 1982

Among the 25 papers included in this volume are a number of studies on the characteristics of cytotoxicity against a variety of tumor cells (animal and human) by macrophages, natural killer (NK) cells and antibody dependent cellular toxicity (ADCC). Many of the papers have important implications for the possible role of these effector cell mechanisms as mediators of biological response modification. Other subjects treated include: the interrelationships of interferon and interferon inducers to enhance NK cell, and ADCC tumor-lytic effect on animal and human tumors, the relationship of prostaglandins and other immunoregulating agents on feedback inhibition mechanisms and suppressor cells which can modify the immune response. One chapter presents a study undertaken to directly investigate the mechanism(s) whereby cytosine arabinoside influences ADCC activity and Fc receptors. (564 Refs)

75. CYTOTOXIC T CELLS IN CYTOMEGALOVIRUS INFECTION. HLA-RESTRICTED T-LYMPHOCYTE AND NON-T-LYMPHOCYTE CYTOTOXIC RESPONSES CORRELATE WITH RECOVERY FROM CYTOMEGALOVIRUS INFECTION IN BONE-MARROW-TRANSPLANT RECIPIENTS.

Quinnan GV, Kirmani N, Rook AH, Manischewitz JF, Jackson L, Moreschi G, Santos GW, Saral R, Burns WH
Div. Virology, Office Biologics, Bureau Drugs and Biologics, Food and Drug Admin., 8800 Rockville Pike, Bethesda, MD, 20205
N Engl J Med; 307(1):7-13 1982

Prospective studies were conducted of cell-mediated cytotoxic response in 58 recipients of syngeneic or allogeneic bone-marrow grafts. Emphasis was placed on the period 4-12 wk after transplantation, when the risk of cytomegalovirus (CMV) infection is greatest. Forty-three patients had CMV during the period of study; 23 patients survived infection. CMV infection was the principal cause of death in 12 patients, and an additional 8 patients died from other causes during acute CMV infection. A significant rise in cytotoxicity was observed early in the course of infection, as measured by CMV-specific cytotoxic lymphocyte response. Evidence of CMV-specific cytotoxic response was found in all patients who survived infection. Patients with nonfatal infections showed significantly greater response than those with fatal infections. The natural-killer-cell activity of lymphocytes from patients with nonfatal infections was within the normal range both before and after the onset of infection, but in the group with fatal infection, lower than normal activity was observed in 4 patients before the onset of infection and in 11 patients afterward. Neither the presence nor level of complement-fixing antibodies in donors or recipients before transplantation correlated with the risk of infection or the likelihood of recovery. The finding that the capacity for cytotoxic response, mediated both by HLA-restricted T lymphocytes and nonrestricted non-T lymphocytes during CMV infection, correlated with recovery strongly suggests that these effector cells mediate recovery from CMV infection. (32 Refs)

76. ABNORMAL IMMUNOREGULATION IN PATIENTS WITH NON-HODGKIN'S MALIGNANT LYMPHOMAS. I. INCREASED HELPER FUNCTION OF PERIPHERAL BLOOD T LYMPHOCYTES.

Gajl-Peczalska KJ, Chartrand SL, Bloomfield CD
Dept. Lab. Medicine and Pathology, Univ. Minnesota, Minneapolis, MN, 55455
Clin Immunol Immunopathol; 23(2):366-378 1982

T lymphocytes isolated from the blood of 24 newly diagnosed and 2 relapsed patients with non-Hodgkin's malignant lymphomas were studied for helper/suppressor activity in cocultures with allogeneic tonsillar B lymphocytes stimulated with pokeweed mitogen. The IgA, IgG, and IgM secretion was measured by double-antibody radioimmunoassay. In 85% of patients with B lymphomas their T lymphocytes produced a severalfold increase in immunoglobulin secretion when compared with age-matched healthy controls. By contrast in two cases of T lymphoma, suppression of immunoglobulin secretion was observed. The ratio of 'T helper'/'T suppressor' lymphocytes, as measured with monoclonal antibodies (OKT4/OKT8), were similar for patients and controls, and concanavalin A-induced suppression was equally good. However, small numbers of patient T lymphocytes provided good help, while control cells failed in these higher dilutions. Possible explanations of the increased helper activity of 'nonmalignant' T lymphocytes in B lymphomas as related to clinical features and the pathogenesis of B- versus T-cell malignancies are discussed. (Author abstract) (31 Refs)

77. MECHANISMS OF TCGF PRODUCTION BY CLONED T-CELL LINES: CHARACTERIZATION OF PRODUCER LYMPHOMA LINES AND KINETICS OF PRODUCTION.

Smith RT, Shimizu S, Norcross MA, Maino VC
Tumor Biology Unit, Dept. Pathology, Univ. Florida, Coll. Medicine, Gainesville, FL, 32610
Clin Immunol Immunopathol; 23(2):286-296 1982

The activation requirements and kinetics of production of T-cell growth factor are described for a stable, cloned T-lymphoma line, EL4-G-12. The line yields a product which has the biochemical and biological attributes of TCGF of normal cell origin examined thus far. Production is dependent upon a transmembrane signal which can be provided by known T-cell-activating lectins, and by antibody to a specific ligand on the Thy-1 molecule, if accessory cells or factors are provided. Production is rapid, beginning within 4 hr, and ceasing between 12 and 18 hr depending upon cell density, signal intensity, and culture conditions. DNA synthesis ceases as production begins, and release is not a result of cell death. It has not yet been determined whether rapid synthesis de novo, or activation and release of an inactive hormone precursor explains the production kinetics observed. (Author abstract) (17 Refs)

78. CYTOGENETIC CHARACTERIZATION OF MOUSE MYELOMA CELL LINES USED FOR PRODUCTION FOR HYBRIDOMAS (MEETING ABSTRACT).

Earley EM
Virology Division, USAMRIID, Fort Detrick, Frederick, MD, 21701
In Vitro; 18(3,part2):296 1982

In 1975 Kohler and Milstein reported the production of monospecific antibodies by fusing mouse spleen cells and cells from a murine continuous myeloma line. The resulting hybrid cells secreted monoclonal antibody into the cell culture medium. Because of the distinct advantages of monospecific antibodies over heterologous antibodies for immunological studies, this new hybridoma technology has resulted in an explosion of reports. It is important for quality control in research to characterize cell lines, particularly continuous cell lines, because of their property of immortality. The myeloma cell line originally used by Kohler and Milstein is designated P3/X63-Ag8, and it secretes immunologlobulins. The resulting hybridomas secrete mixtures of light and heavy immunoglobulin chains of both parental cells. Therefore, several clones were selected from the P3 parental line. The clone designated NS-1 secretes only kappa light chain; whereas clone 653, a second line, does not secrete any immunoglobulin. In addition, a third line, SP2/0, is frequently used for fusion. I have been analyzing these mouse myeloma cell lines by C-banding and nucleolar organizer region (NOR) techniques to identify marker chromosomes. Using these characterization studies, I identified contamination of one myeloma parental cell line by a hybridoma line. (no Refs)

79. THE EPIDEMIC OF ACQUIRED IMMUNE DYSFUNCTION IN HOMOSEXUAL MEN AND ITS SEQUELAE. OPPORTUNISTIC INFECTIONS, KAPOSI'S SARCOMA, AND OTHER MALIGNANCIES: AN UPDATE AND INTERFRETATION.

Levine AS

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Cancer Treat Rep; 66(6):1391-1395 1982

Incidence of pneumocystis carinii pneumonia (PCP) and Kaposi's sarcoma (KS), survival, risk factors, immune dysfunction, genetics, course of the illness, and treatment are reviewed. Three-hundred patients (290 men) with a new syndrome have been reported; 135 had CP, 115 KS, 28 both diseases, and 22 other opportunistic infections. The mortality rate has been 40%; however, greater than 70% of patients with earliest diagnosed cases have died. Eighty-five percent of the 300 patients have been less than 45 yr old, with a median of 35 yr. Of the 290 men, 242 have been homosexual or bisexual. Ninety-eight percent of the homosexual male patients have had a history of exposure to nitrites, mainly amyl or butyl inhalants, but no one nitrite preparation is over-reported, suggesting that whatever the involvement of nitrites in the syndrome is not due to a contaminant. A very extensive case-control study will be required to sort out the relative contributions of nitrites and transmissible microbes; independent risk factors may be impossible to be identified. The breadth of immune defects observed in the syndrome explains the broad gap in host defenses against all classes of microbes that are associated with cellular immunity. The possibility exists that once the patients have become immunodeficient, a considerable reactivation of the cytomegalovirus infection occurs. As many as one third of KS patients in the epidemic appear to be developing other malignancies, as occurs with other KS patients, including the sporadic and endemic patients and the patients in renal transplant recipients or in patients receiving chronic immunosuppressive therapy. (17 Refs)

80. DISTINCT SUPPRESSOR CELL POPULATIONS IN SPLEENS OF TUMOUR BEARING MICE (MEETING ABSTRACT)

Howie S, McBride WH

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Twenty-third Annual General Meeting of the British Association for Cancer Research, March 29-31, 1982, Edinburgh, Scotland. British Association for Cancer Research 78 pp., 1982.

Spleens of tumor bearing mice contain tumor specific T helper cells which will collaborate with hapten primed B cells to induce specific antibody formation in vitro. Helper activity disappears when the tumor is large. This loss of helper activity is coincident with the appearance of two distinct types of suppressor cells a) nylon-wool-non-adherent T cells which are tumor specific and b) nylon-wool-adherent non-T cells which are not specific in their action. (no Refs)

81. THE ULTRASTRUCTURAL LOCALIZATION OF IMMUNOGLOBULINS IN HUMAN B CELLS OF IMMUNOPROLIFERATIVE DISEASES.

Gourdin MF, Farcet JP, Reyes F

(c/o Reyes) INSERM U.91, Hopital Henri Mondor, 94010 Creteil, France

Blood; 59(6):1132-1140 1982

The cellular distribution of immunoglobulins in human malignant and normal B cells was investigated by immunoelectron microscopy by direct incubation of fixed cells with peroxidase-coupled antibody. These conjugates penetrated into the cell, resulting in the simultaneous detection of surface and cytoplasmic immunoglobulins. The latter were seen as specific intracisternal staining of the perinuclear space and endoplasmic reticulum and occasionally of the Golgi complex. Plasma cells were frequently characterized by a heterogeneity of reactivity of the endoplasmic reticulum. Minute amounts of cytoplasmic immunoglobulin were demonstrated in cells without developed secretory organelles, such as lymphoma cells and lymphocytes from chronic lymphocytic leukemia (CLL). The method allowed us to define several subsets of cells according to the expression of surface and cytoplasmic immunoglobulins and thus to determine the stage of maturation of cells involved in monoclonal proliferation. (Author abstract) (36 Refs)

82. THE OCCURRENCE OF CANCER IN IMMUNE DEFICIENCIES.

Penn I
Dept. Surgery, Univ. Colorado Health Sciences Center, Denver, CO
Curr Probl Cancer 6(10): 64 pp., 1982.

The association of immune deficiency states with increased cancer risk is discussed in detail. Topics covered include components of the immune system (specific immune responses, B cells, T lymphocytes, delayed hypersensitivity cells, cytotoxic T cells, helper T cells, and suppressor T cells), immune amplification mechanisms, nonspecific responses (humoral response, cellular response), immune responses to cancer (reactions deleterious to tumor growth, reactions favoring tumor growth [blocking factors, fetal antigens, alpha2-globulins, small mol wt immunosuppressive factors, suppressor cells, lack of complement]). Also discussed are mechanisms by which tumors escape immune destruction by the host, cancer in immunodeficient states, naturally occurring immunodeficient states, changes associated with organ transplantation (immunosuppressive therapy, transplanted malignancies, cancers arising de novo after organ transplantation [incidence, age and sex of patients, time of appearance of cancers, previous tumors in recipients, malignancies in the donors, types of malignancy]), multiple cancers, treatment, prognosis, effects of immunosuppression on preexisting neoplasms, cancer in uremic patients, second neoplasms arising in patients after cancer chemotherapy and radiotherapy, etiology of neoplasms in immunodeficient states, spontaneous regression of lymphomas, interferons, oncogenic viruses, oncogenic and co-oncogenic effects of immunosuppressive and cancer chemotherapeutic agents, and other potentially oncogenic treatments. (265 Refs)

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TUMOR ANTIBODY PRODUCTION/ CHARACTERIZATION/ DETECTION

1. DETECTION OF ANTIBODY TO CARCINOEMBRYONIC ANTIGEN BY THE HEMOLYTIC PLAQUE ASSAY.

Stinson RS, Lockhart CG, Margraf HW, Philpott GW

Dept. Microbiology, Univ. Alabama, PO Box BM, University, AL, 35486

Int Arch Allergy Appl Immunol; 68(2):134-137 1982

A modification of the standard hemolytic plaque-forming cell assay is described. The conjugation of a soluble antigen, carcinoembryonic antigen, to the membrane of the sheep red blood cell was accomplished and used as the indicator system to detect antibody-forming cells. The specificity of the assay was determined by cross-reacting studies and competitive inhibition by antigen blocking. (Author abstract) (15 Refs)

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2. MONOCLONAL ANTIBODY (IGM) SPECIFIC TO MOUSE LYMPHOMA CELLS (L 1210): ISOLATION AND THERAPEUTIC PROPERTIES.

Roche AC, Monsigny M
Laboratoire de Biochimie cellulaire et moleculaire des Glycoconjugues, Centre de Biophysique Moleculaire, C.N.R.S., 1A, avenue de la Recherche Scientifique, 45045 Orleans Cedex, France
Cell Biol Int Rep; 6(6):557-565 1982

The characterization of an IgM monoclonal antibody reacting with a L 1210 cell line is described as well as its use in therapy of transplanted L 1210 leukemia in mice. Balb/C mice were immunized by injection of live L 1210 cells. Splenocytes from two of the mice which had a high serum anti-L 1210 titer were fused with SP2-O-Ag myeloma cells. Hybridoma clones which produced anti-L 1210 antibodies were selected on the basis of cytolysis induced in the presence of rabbit complement. Active antibodies were obtained by gel filtration chromatography on Ultrogel AcA 34. The first peak contained a pure IgM as shown by immunodiffusion and was well-separated from other serum proteins. These antibodies were not themselves cytotoxic, and did not induce cytolysis of L 1210 cells in the presence of autologous serum. Antitumor activity of IgM antibodies was tested in vivo in BDF1 mice inoculated with L 1210 cells. Passive immunotherapy with IgM monoclonal antibodies (2.4 mg/mouse) resulted in prolonged survival and a significant proportion of treated mice were cured. (14 Refs)

3. ENRICHED NATURAL KILLING AND ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY IN LYMPHOCYTE POPULATIONS ADHERENT TO TUMOR CELL MONOLAYERS.

Jensen PJ, Koren HS
NCI-Frederick Cancer Res. Facility, P. O. Box B, Frederick, MD, 21701
Immunobiology, 161(5):494-506 1982

We have previously shown that human peripheral blood lymphocytes that do not adhere to natural killer (NK)-sensitive target cell monolayers are at least partially depleted of NK activity. To demonstrate directly that NK effector cells adhere to the monolayers, we have now recovered the adherent populations by treatment with ethylenediaminetetraacetic acid. When tested immediately after isolation, these adherent populations show NK activity that is intermediate between that of the nonadherent and control cells. When antibody-dependent cellular cytotoxicity is tested concomitantly, the adherent fractions are consistently found to be enriched relative to control, unfractionated lymphocytes. In further studies, control populations and fractions nonadherent and adherent to HSB monolayers are incubated overnight at 37 C and then tested for NK activity. We find that the adherent fractions are selectively enhanced in activity, causing the NK activity of the adherent fractions to exceed that of control populations. The possible involvement of interferon in the augmentation of NK activity is considered. (Author abstract) (34 Refs)

4. IN VITRO PRODUCTION OF MONOCLONAL AND POLYCLONAL IMMUNOGLOBULINS BY PERIPHERAL BLOOD MONONUCLEAR CELLS IN HUMAN PLASMA CELL MYELOMA.

Peest D, Holm G, Mellstedt H, Pettersson D
Klinische Immunologie, Medizinische Hochschule Hannover, Postfach 610180, D 3000 Hannover 61, W. Germany
Scand J Immunol; 15(6):595-603 1982

The in vitro monoclonal and polyclonal immunoglobulin (Ig) production of peripheral blood mononuclear cells was studied in human multiple myeloma (4 IgG myelomas, 1 IgA myeloma) and in one patient with benign monoclonal gammopathy. Using an enzyme-linked immunosorbent assay with anti-class-specific antisera and antisera against idiotypic structures on the myeloma protein, it was possible to quantitate separately monoclonal and polyclonal Ig of the same class in cell culture supernatants. After stimulation with pokeweed mitogen (PWM) patients' cells produced lower amounts of polyclonal Ig than cells from healthy adults. In contrast, production of monoclonal Ig could not be enhanced by PWM. Moreover, the kinetics of monoclonal Ig production was different from that of polyclonal Ig. Myeloma cells contained large amounts of monoclonal Ig while their content of polyclonal Ig was low. A rapid release of preformed monoclonal Ig during the 1st day of culture was not inhibited by puromycin. A later phase of release was partly suppressed by puromycin and was probably caused by active protein synthesis. (Author abstract) (27 Refs)

5. IN VIVO LOCALIZATION OF ANTI-OSTEOGENIC SARCOMA 791T MONOCLONAL ANTIBODY IN OSTEOGENIC SARCOMA XENOGRAFTS.

Pimm MV, Embleton MJ, Perkins AC, Price MR, Robins RA, Robinson GR, Baldwin RW
Cancer Res. Campaign Lab., Univ. Nottingham, Nottingham, NG7 2RD, England
Int J Cancer; 30(1):75-85 1982

Monoclonal antibody 791T/36, (mouse IgG2b) to the human osteogenic sarcoma 791T was isolated from hybridoma supernatants or ascites fluid and labelled with radioiodine. Following injection into immuno-deprived CBA mice with subcutaneous xenografts of human osteogenic sarcomas 791T, 788T and 20s, reactive antibody was detectable in the circulation and there was a preferential uptake into tumor tissue compared with muscle, bone or visceral organs. The tumor uptake of radioactivity correlated with the size of the xenograft, up to 20% of the total body counts being within the tumor. Autoradiography of tissue sections showed activity mainly within the subcapsular regions of the xenografts. There was no tumor localization of radio-labeled normal IgG. Furthermore, with a colon carcinoma and a bladder carcinoma, both unreactive with the 791T/36 antibody, there was no localization of radiolabeled antibody in xenograft growths. With 791T/36 monoclonal antibody labeled with 131I localization into 791T xenografts could be visualized by whole-body gamma scintigraphy with computerized 99mTc-pertechnetate or 113mIn-indium chloride-labeled blood pool subtraction. These studies demonstrate the potential of monoclonal antibody to a human tumor for in vivo localization both for diagnostic purposes and as a carrier for therapeutic agents. (Author abstract) (28 Refs)

6. NATURALLY OCCURRING ANTIBODIES AGAINST FIBROSARCOMA AND GLIOMA CELLS IN RATS.

Itaya T, Moriuchi T, Kodama T, Sendo F, Kobayashi H
Lab. Pathology, Cancer Inst., Hokkadio Univ. Sch. Medicine, Kita-15-jo Nishi-7-chome, Kita-ku, Sapporo 060, Japan
Gan; 73(3):454-461 1982

The presence of natural antibodies (NA) against fibrosarcoma and glioma cells was detected in the normal sera of 10 different strains of rats. By means of a complement-dependent cytotoxicity test and an absorption test, the NA-reactive antigens were detected in all investigated syngeneic and allogeneic fibrosarcoma lines and one glioma line, but not in hepatoma, lymphoma, leukemia, and neurinoma lines. Moreover, the cytotoxic activity of NA was significantly absorbed by normal brain, lung, kidney, skin homogenates, and cultured fibroblasts

of syngeneic rats, but not by liver homogenates, thymus, spleen, lymph node or red blood cells. With the exception of a Donryu rat strain, there were no strain or sex differences in the NA levels among the investigated strains of rats. The NA were biochemically identified as being IgM and were stable at 56 C for 30 min. The level of NA correlated with the in vivo antitumor response: when NA-reactive fibrosarcoma or glioma cells were implanted into syngeneic WKA/Hok rats, groups of rats with high NA levels showed suppression of tumor growth and prolongation of survival time as compared to groups of rats with low NA levels, while there was no difference in survival time of rats transplanted with NA non-reactive hepatoma or lymphoma lines. When 3-methylcholanthrene was inoculated into rats, the tumor incidence in the group of rats with high NA levels was significantly suppressed as compared to the group of rats with low NA levels. (Author abstract) (18 Refs)

7. AUTOLOGOUS ANTIBODIES AGAINST LEUKEMIA CELLS.

Pfreundschuh M, Dorken M, Ho AD, Korbling M, Hunstein W
Med. Univ.-Poliklinik Heidelberg, Heidelberg, W. Germany
Verh Dtsch Ges Inn Med; (87):727-729 1981

Twenty patients with acute lymphatic or acute nonlymphatic leukemia were tested for autologous antibodies (AA) against leukemia cells. Serum was obtained when possible before and during therapy. Antibodies were measured using immune adherence, protein-A, and anti-C3-mixed hemadsorption assays. For six of the patients the tests for AA were negative by all three assays; for the remaining patients titers varied from 1:2 to 1:64. The specificity of these antibodies for leukemia cells was considered to be uncertain. No correlation was found between antibody titers and stage of therapy. (17 Refs) (In GER)

8. MONOCLONAL ANTIBODIES AGAINST SURFACE ANTIGENS OF LARYNGEAL CARCINOMA CELLS. A NEW EXPERIMENTAL APPROACH FOR THE EARLY DIAGNOSIS AND IMMUNOTHERAPY.

Zenner HP, Herrmann IF, Schimpl A
Dept. Otolaryngology, Univ. Wurzburg, Wurzburg, W. Germany
Excerpta Med Int Congr Ser; 582:141-146 1982

Use of monoclonal antibodies against surface antigens of laryngeal carcinoma cells as an approach for early diagnosis and immunotherapy is reported. The outer cell membranes of tumor cells can be broken down in their protein components by polyacrylamide gel electrophoresis. A radioimmunoassay was used to demonstrate that 47/50 laryngeal cancer patients formed antibodies to their own tumors. Of 52 patients examined, 20% possessed IgG-antibodies which cross reacted with the isolated carcinogenic cells from a single patient. A model of surface antigens in laryngeal carcinomas was proposed. Most surface antigens can be detected in both normal and malignant cells, however, tumor cells lack certain surface characteristics; other antigens are found only in tumor cells. Xenogeneic antibodies were used to prepare monoclonal antibodies for clinical studies. Clones were produced from myeloma cells crossed with antibody producing splenic cells. Seventy-three clones capable of forming anti-laryngeal antibodies were identified. The monoclonal antibody identifies various malignant target cells, including two laryngeal carcinomas and two salivary gland carcinomas. Immunofluorescence studies demonstrated that the monoclonal antibodies used can differentiate tumor tissue from non-tumor tissue. Using monoclonal antibodies as reported groups, a single cell which is not identifiable as malignant or not could be shown to possess antigens corresponding to the serum. (5 Refs)

9. MONOCLONAL ANTIBODIES TO A HUMAN PROSTATE ANTIGEN.

Frankel AE, Rouse RV, Wang MC, Chu TM, Herzenberg LA

Cetus Immune Corporation, 3400 West Bayshore Drive, Palo Alto, CA, 94305

Cancer Res; 42(9):3714-3718 1982

Three monoclonal antibodies reactive with a purified extractable Mr 34,000 prostate antigen (PA) have been prepared by fusing splenocytes of BALB/c mice preimmunized with purified PA with the NS1 mouse myeloma cell line. The three antibodies were all of the IgG-1 subclass. The antibodies defined two noncross-blocking unique determinants on PA; each present as one site per molecule. IF3 defined on antigenic site and 2G7 and 1C5 defined another antigenic determinant. All of the antibodies reacted with PA in a solid-phase radioimmunoassay and immunoprecipitated 125I-labeled PA. Absorption and sandwich radioimmunoassays showed PA in prostate tissues but not in tonsil, liver, or kidney. Immunoperoxidase staining of formalin-fixed paraffin-embedded sections of benign prostatic hyperplasia and prostatic carcinoma revealed strong prostate epithelial reactivity. None of the antibodies showed reactivity with prostate membrane preparations. A sandwich radioimmunoassay used 2G7 as a plate coat. 125I-labeled 1F3 was used to detect 5 ng PA per ml in sera of patients with prostate cancer. These results confirm previous observations regarding the specificity of PA and shed new evidence for its intracellular localization. (Author abstract) (17 Refs)

10. PRODUCTION OF A TUMOR-SPECIFIC XENOANTISERUM FROM PARTIALLY PURIFIED IMMUNOPROTECTIVE TUMOR ANTIGEN.

Tanaka T, Yamagishi H, Pellis NR, Kahan BD

(c/o Pellis) Dept. Surgery, Div. Organ Transplantation, Univ. Texas Medical Sch. at Houston, Houston, TX, 77030

Cancer Immunol Immunother; 13(1):48-52 1982

Raising of specific xenoantisera in rabbits by purified tumor-specific transplantation antigens (TSTA) preparations was studied. Serum from the rabbit immunized with partially purified 3-methylcholanthrene (MCA)-F tumor TSTA (fraction 15, Fr 15) displayed a complete or semi-circular ring reaction in the immunofluorescence assay at a titer of 1:4 when a fluorescein isothiocyanate-conjugated goat anti-rabbit IgG serum was used at a dilution of 1:8. Absorption with 10(8) intact MCA-F cells diminished the ability of 1 ml anti-Fr 15 serum to bind MCA-F cells by 95%. On the other hand, absorption with MCA-D or MCA-T cells did not significantly inhibit the immunofluorescence reaction. Preincubation with 30 mg 3 M KCl extract or with 7.5 mg Fr 15 completely inhibited the binding capacity of 1 ml anti-Fr 15 serum. No significant difference in the fluorescence between cells stained after 5-hr incubation at 37 C and cells stained immediately was observed. Thus neither macrophages nor other Fc receptor-bearing cells significantly contributed to the proportion of tumor-derived cells exhibiting fluorescence. The xenoantibody displayed specific immunologic reactivity in the indirect membrane immunofluorescence assay, suggesting that administration of purified materials may afford new reagents with which to dissect and purify TSTA. (23 Refs)

11. MONOCLONAL ANTIBODIES TO CARCINOEMBRYONIC ANTIGEN (CEA): CHARACTERIZATION AND USE IN A RADIOIMMUNOASSAY FOR CEA.

Lindgren J, Bang B, Hurme M, Makela O
Wistar Inst., 36th St. at Spruce, Philadelphia, PA, 19104
Acta Pathol Microbiol Immunol Scand [C]; 90(3):159-162 1982

Fusion of immune spleen cells of mice immunized with CEA with a mouse myeloma cell line resulted in several hybrid cell lines secreting antibodies to CEA as tested by radio-immunoassay. Four of these were cloned by limiting dilution and large amounts of anti-CEA antibodies were produced by growing the anti-CEA-producing cell clones intraperitoneally in mice and collecting the ascites fluids formed. Ascites fluids containing antibodies with both high and low affinity were obtained. The antibody having the highest affinity was shown to be specific to CEA, whereas one antibody showed crossreaction with the normal cross-reacting antigen (NCA). The establishment of a competitive-inhibition double antibody radio-immunoassay with high sensitivity and specificity using mouse monoclonal antibodies is described. (Author abstract) (15 Refs)

12. MONOCLONAL IMMUNOGLOBULIN OF CLL LYMPHOCYTES DETECTED BY RADIOIMMUNOFIXATION WITH 125I-PROTEIN A OF TRITON X-100 SOLUBILIZED LYMPHOCYTE MATERIAL.

Plesner T, Wilken M, Bjerrum OJ, Hansen MM
Dept. Clinical Chemistry, Finsen Inst., DK-2100 Copenhagen, Denmark
J Clin Lab Immunol; 8(2):137-141 1982

Triton X-100 solubilized material from isolated chronic lymphocytic leukemia (CLL)-lymphocytes obtained from 32 previously untreated patients with CLL was studied using immunofixation with 125I-protein A. The increase in sensitivity obtained by radiolabeling with 125I-protein A was comparable to that observed in other radioimmuno-electrophoretic systems. Two complete IgM type M-components were demonstrated in two patients, an excess of apparently free heavy chains in four, and an excess of apparently free light chains in six. (28 Refs)

TUMOR ANTIBODIES ASSOCIATED WITH VIRUSES

13. INTERACTION OF EPSTEIN-BARR VIRUS WITH LEUKAEMIC B CELLS IN VITRO. II. CELL LINE ESTABLISHMENT FROM PROLYMPHOCYTIC LEUKAEMIA AND FROM WALDENSTROM'S MACROGLOBULINAEMIA.

Finerty S, Rickinson AB, Epstein MA, Platts-Mills TA
Dept. Pathology, Medical Sch., Univ. Bristol, Bristol, England
Int J Cancer; 30(1):1-7 1982

Leukemic B-cell populations were prepared from six patients with high-count prolymphocytic leukemia (PLL) as well as from one patient with Waldenstrom's macroglobulinemia (WM) in frankly leukemic phase, and their response to in vitro Epstein-Barr (EB) virus infection was monitored in terms of expression of the virus-associated nuclear antigen EBNA and of virus-induced transformation to continuous cell lines. The individual leukemic populations, tested on several occasions, gave reproducibly different responses one from another which were not obviously related to differences either of surface immunoglobulin phenotype or of immunoglobulin secretor status in vivo. After infection, four out of six PLL populations showed either transient or a more persistent expression of EBNA, always involving a minority of the cells, with no evidence of any virus-induced transformation up to 6 wk. In contrast, two out of six PLL samples as well as the WM sample rapidly gave rise to EBNA-positive cell lines which, on the evidence both of restricted immunoglobulin class expression and of abnormal marker chromosomes, were clearly derived from the leukemic cells. Further comparative studies of such leukemic B-cell populations may help to define host cell components necessary for the triggering of EB-virus-induced cellular transformation. (Author abstract) (32 Refs)

14. HEPATITIS B VIRUS AND PRIMARY HEPATOCELLULAR CARCINOMA: FAMILY STUDIES IN KOREA.

Hann HW, Kim CY, London WT, Whitford P, Blumberg BS
Inst. Cancer Res., Fox Chase Cancer Center, Philadelphia, PA, 19111
Int J Cancer; 30(1):47-51 1982

Chronic infection with hepatitis B virus (HBV) is closely associated with the etio-pathogenesis of primary hepatocellular carcinoma (PHC). It has been proposed that infection with HBV early in life, frequently transmitted by an HBV-carrier mother, leads to persistent infection with HBV, which in turn is associated with the development of chronic active hepatitis (CAH), post-necrotic cirrhosis and PHC. If this view is correct, then there should be clustering of chronic carriers of HBV in families of patients with chronic liver disease. We tested this hypothesis in Korea by collecting serum from 132 patients with these chronic liver diseases admitted to the Seoul National University Hospital and 664 of their first-degree relatives. Sera were assayed for hepatitis B surface antigen (HBsAg), antibody to HBsAg (anti-HBs) and antibody to hepatitis B core antigen (anti-HBc). Almost all cases showed evidence of present or past infection with HBV. Mothers of patients were more frequently HBsAg(+) than age-matched women in the control population or wives of patients. Five of 23 fathers were also HBsAg(+) compared with 1 of 25 age-matched controls. There was a deficit of anti-HBs in the fathers of cases compared with the controls. Siblings of patients were frequently HBsAg(+), with the highest prevalence in brothers. Family history shows that five fathers, two mothers and five brothers of cases have died of PHC. These data are compatible with the hypothesis tested and lend further support to the view that prevention of infection with HBV will lead to a marked decrease in the incidence of CAH, cirrhosis and PHC in areas where these diseases are endemic. Members of the families of patients with these diseases are at high risk of developing persistent infection with HBV and chronic liver disease. It would be appropriate to focus preventive strategies on infants and children in such families. (19 Refs)

15. IMMUNE STIMULATION OF SENSITIZED CHICKEN LYMPHOCYTES BY AVIAN RETROVIRUS PROTEINS.

Wainberg MA, Israel E
Lady Davis Inst. for Medical Res., Sir Mortimer B. Davis Jewish General Hosp., 3755 Cote Sainte Catherine Road, Montreal Quebec, H3T 1E2, Canada
J Gen Virol; 60(part2):391-395 1982

Peripheral blood lymphocytes of chickens bearing tumors induced by avian sarcoma virus can be specifically stimulated to divide by the crude culture fluids of virus-infected cells. In this communication, we show that relevant antigenic activity apparently resides in each of the internal virus proteins p15 and p27. The ability of infectious culture fluids to be mitogenic for sensitized lymphocytes is greatly reduced following treatment with antibodies specific for either total avian myeloblastosis virus (AMV) protein or for p27. (Author abstract) (14 Refs)

16. HUMORAL IMMUNE RESPONSE IN EPSTEIN-BARR VIRUS INFECTIONS. I. ELEVATED SERUM CONCENTRATION OF THE IGG1 SUBCLASS IN INFECTIOUS MONONUCLEOSIS AND NASOPHARYNGEAL CARCINOMA.

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Clin Exp Immunol; 49(1):149-156 1982

Using radial immunodiffusion we measured IgG subclass concentrations and studied their distribution in serum samples from patients with infectious mononucleosis (IM) and nasopharyngeal carcinoma (NPC), two Epstein-Barr virus (EBV)-associated diseases, in comparison with two control groups [completely anti-EBV negative persons and subjects carrying antibodies to the viral capsid antigen (VCA)]. Antibody titers to VCA and to the early antigen (EA) were determined by indirect immunofluorescence and revealed characteristic patterns for the respective diagnostic groups. Nephelometric assays served for quantitating total protein, albumin, total IgG, IgA and IgM in all the sera. In the IM and NPC groups the concentration of IgG1 was significantly elevated by more than 50% whereas the other three subclasses remained unchanged as compared with the controls. Correspondingly, we found a significant increase of total IgG in IM and NPC. In IM, the only disease where VCA-specific IgM antibodies have been reported to occur, IgM levels were markedly elevated. Our data suggest that the IgG1 subclass plays an important role in the humoral immune response to EBV-determined antigens and that it is possibly involved in the control of virus infection. (Author abstract) (24 Refs)

17. SEROLOGIC TESTS FOR NASOPHARYNGEAL CARCINOMA IN NORTH AMERICAN PATIENTS.

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Excerpta Med Int Congr Ser; 582:111-114 1982

The clinical value of serum titers of various Epstein-Barr virus (EBV) related antibodies was investigated in 92 North American patients with primary nasopharyngeal carcinoma (NPC), 149 patients with head and neck cancer (HNC) other than nasopharyngeal, 342 patients with benign diseases (BD) commonly seen in large otolaryngologic practices, and 100 healthy blood donors. Antibody titers of sera from patients with untreated NPC differed significantly from those of the other groups. Positive titers for the IgA anti-viral capsid antigen were found in 70% of NPC patients, only 5% of those with HNC, and 10% of those with BD. Undifferentiated and nonkeratinizing carcinomas consistently exhibited elevated antibody titers directed against viral capsid antigen and early antigen. The incidence of elevated titers was lower in patients with keratinizing squamous cell carcinoma compared with the other groups. The incidence of positive IgA anti-viral capsid antigen titers in undifferentiated and nonkeratinizing varieties were much greater than those in keratinizing squamous cell varieties. A trend toward higher antibody titers with the development of metastases was seen. Of the 13 patients who died, 8 had low antibody-dependent cellular cytotoxicity titers at diagnosis and 4 had high titers. In general, patients with very high antibody-dependent cellular cytotoxicity titers remained free of disease for as long as 4 yr; these patients should be followed closely in order to determine the prognostic value of the EBV markers. (5 Refs)

18. HEPATITIS A VIRUS INFECTION OF HBSAG-PRODUCING HEPATOCELLULAR CARCINOMAS IN ATHYMIC MICE.

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Cancer Immunol Immunother; 13(1):53-55 1982

Response of athymic mice bearing tumors of hepatocellular carcinoma (HCC) origin to infection with hepatitis A virus (HAV) and the production of HAV antigen (HAAg) in vivo were examined. Tumors were observed 25 days after inoculation in 17/23 mice when more than 2 x 10(7) PLC/PRF/5 or Hep 3B cells (of HCC origin) were injected. Histological examination of the tumors (originated by cell inoculation or tissue transplantation) revealed a morphology similar to that of differentiated primary HCC tumors. Neither antigens nor antibodies of the HBc or HBe system could be detected, but HBsAg or anti-HBs were found. (hepatitis B surface antigen) or anti-HBs were found. Sera of all mice bearing tumors were also positive for alpha-fetoprotein. PLC/PRF/5 cells in monolayer culture were infected with cell culture-adapted HAV. After 5 wk, when HAAg could be detected, the infected cells were suspended and inoculated into nude mice at a concentration of 5 x 10(7) cells/mouse. Only one of three mice developed a small nodule (100 mg wet wt) which was positive for HAAg. After transfer of tumor pieces to another series of mice, no mice grew tumors within 4 wk. Infectious virus (105TCD50) was inoculated directly into existing tumors. HAAg was found in six of eight inoculated tumors after 16-37 days. No significant relationship was observed between HAV injection and tumor growth in animals. When sera of HAV-infected tumor-bearing mice were tested for markers of HAV, neither antigen nor antibody was detected. (11 Refs)

19. IMMUNOLOGY AND DIAGNOSIS OF NASOPHARYNGEAL CARCINOMA.

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Excerpta Med Int Congr Ser; 571:389-397 1982

Results of a series of studies are discussed to assess the value of testing for some Epstein-Barr virus (EBV)-specific serologic and immunologic markers in the diagnosis of nasopharyngeal cancer (NPC). All the sera tested were from Chinese patients and residents in Hong Kong. The sera were titrated for IgA and IgG antibodies to viral capsid antigen (VCA) and early antigen (EA) of EBV by the indirect immunofluorescent technique. The first study showed that NPC patients have a broader spectrum and higher geometric mean titer (GMT) of serum antibodies to EBV-specific antigens than do patients with other tumors of the respiratory and upper aerodigestive tracts and healthy subjects. A second study established that there was a stepwise rise in the GMT for all four antibodies with advancing stages of disease (I-IV). A further study was done to assess the value of titration of the four antibodies in the diagnosis of NPC. IgA to VCA had the highest sensitivity with a detection rate of 95% and relatively high specificity. IgA to EA was highly specific with no false positives but a detection rate of only 78%. IgG to VCA was the least discriminatory, while EgG to EA fell between IgA to EA and IgG to VCA. An ongoing study involves the evaluation of the titration of serum IgA to VCA as a screening test for NPC in its early presymptomatic stage in subjects known to have a high risk of the disease, namely, close blood-linked relatives of Chinese NPC patients. In these patients, if the serology is suggestive, multiple nasopharyngeal biopsies are indicated. Data are presented on serum EBV-specific antibody titers in four siblings initially and at time of diagnosis of NPC. (17 Refs)

20. A PRELIMINARY STUDY ON THE ANTI-EBV-SPECIFIC DNASE ACTIVITIES OF NASOPHARYNGEAL CARCINOMA (NPC) PATIENTS' SERA.

Pan Q, Huang D, Luo W, Jiao X, Chen J, Chen L
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Excerpta Med Int Congr Ser; 571:418-422 1982

An anti-DNase activity was demonstrated in the sera of patients in various stages of nasopharyngeal cancer (NPC). A combination of n-butyric acid (4 milliM) and croton oil (400 nanog/ml) was used to induce Epstein-Barr virus (EBV)-specific DNase in EBV-genome-containing cell lines Raji and PeHR-1. An assay utilizing 14C-DNA was devised to determine the effect of NPC patients' sera on the DNase activity of the cell homogenate. Because of the presence of an antibody in the sera of NPC patients, and the neutralizing effect of this antibody to the enzyme, addition of patients' sera markedly decreased the DNase activities to give anti-enzyme rates of 52-55%. The level of serum anti-enzyme activity varied from NPC patient to patient. There appeared to be a good parallelism between the anti-enzyme activity of the serum and its titer to viral capsid antigen to IgA. Further studies are in progress to confirm the practical value of this enzymological test for early detection of NPC. (5 Refs)

21. PERSISTENT ACTIVE INFECTION OF EPSTEIN-BARR VIRUS (EBV) IN CARRIER FEMALES OF THE X-LINKED LYMPHOPROLIFERATIVE SYNDROME (XLP).

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Excerpta Med Int Congr Ser; 571:375-379 1982

Among conditions that may follow infection with Epstein-Barr virus (EBV), is malignant lymphoma in males affected by the X-linked lymphoproliferative syndrome (XLP). To test the hypothesis that the variable expression of XLP is manifested in obligate carrier females, blood from 12 obligate carrier females was studied for anti-viral capsid antigen (VCA), anti-early antigen (anti-EA) and anti-Epstein-Barr nuclear-associated antigen (EBNA). All carriers were seropositive to EBV. The reciprocal geometric mean titer for IgG anti-VCA was elevated to 570 in the carrier females compared to 100 in 24 controls. The range of anti-VCA was from 80 to 5,120. IgA class anti-VCA was found in 2/3 of the carriers. All but one of those with anti-VCA of IgA class showed anti-EA, indicative of active infection and immunodeficiency. About one-half of the carriers had persistent anti-EA antibodies. However, the anti-EBNA levels of carrier females were similar to those of the healthy controls. There was no apparent relationship between IgM level and EBV-specific antibody titers. The paradoxically elevated EBV-specific antibodies which tend to persist in obligate carriers of XLP provides an opportunity to define the immunopathology of XLP and to detect carrier females. (17 Refs)

22. CYTOMEGALOVIRUS AND KAPOSI'S SARCOMA IN YOUNG HOMOSEXUAL MEN.

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Lancet; 2(8290):125-127 1982

Ten homosexual men with Kaposi's sarcoma (KS) were studied for evidence of cytomegalovirus (CMV) infection. IgG and IgM antibodies to CMV were detected in nine out of nine and in seven out of nine of these patients, respectively. CMV was recovered from body secretions or peripheral blood of seven patients. Viral cultures of KS tumor biopsy specimens were negative in eight out of eight patients, but CMV RNA was detected by in-situ hybridization in two out of three and CMV antigen(s) by immunofluorescence in six out of nine. Normal tissue specimens from three KS patients were negative for CMV antigen. These observations suggest an association of CMV with KS. (Author abstract) (25 Refs)

23. SEROLOGICAL STUDIES ON NASOPHARYNGEAL CARCINOMA AND CERVICAL CANCER IN CHINA.

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Excerpta Med Int Congr Ser; 571:380-388 1982

A serological study on Epstein-Barr virus (EBV) infection was performed in areas of high and low risk for nasopharyngeal cancer (NPC). A micro-complement fixation test for antibody to EBV in sera of 2,300 normal individuals of all ages indicated a positive reaction in 90-100% of children aged 3-5 yr. The geometric mean titer (GMT) from the healthy population over age 20 was significantly higher in areas of high NPC risk. This type of variation may reflect reactivation of EBV in people living in the NPC high risk area and which might be related to the occurrence of NPC. Results of serologic mass surveys of NPC are reported in Zangwu county in 1978-1980. The incidence of antibody to herpes simplex virus (HSV) 1 and 2 was determined in normal women in both a high- (Jienan county) and a low-risk (Beijing) area for cervical cancer and in patients. There was no marked difference in frequency of antibody to HSV-1 in the cervical cancer patients and in the controls from high and low risk areas. However, in the cervical cancer group, the GMT of antibody to HSV-1 was a little higher than that in the control group; this may be due to cross-reaction to antigen between HSV-1 and HSV-2. A study of age-specific incidence of HSV infection in areas of high and low cervical cancer risk indicates a relationship between early and severe infection of HSV-2 and high risk of cervical cancer. While the age-specific incidence of HSV-2 infection in China is similar to that in some western countries, the social system and life-style are quite different, indicating some other mode of infection than venereal transmission. (22 Refs)

24. EPSTEIN-BARR VIRUS-INDUCED DISEASES IN BOYS WITH THE X-LINKED LYMPHOPROLIFERATIVE SYNDROME (XLP). UPDATE ON STUDIES OF THE REGISTRY.

Purtilo DT, Sakamoto K, Barnabel V, Seeley J, Bechtold T, Rogers G, Yetz J, Harada S, XLP Collaborators
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Am J Med; 73(1):49-56 1982

Analyses of 100 subjects with the X-lined lymphoproliferative syndrome (XLP) in 25 kindreds revealed four major interrelated phenotypes: infectious mononucleosis, malignant B-cell lymphoma, aplastic anemia, and hypogammaglobulinemia. Eighty-one of the patients died. Two male subjects were asymptomatic but showed immunodeficiency to Epstein-Barr virus (EBV). Seventy-five subjects had the infectious mononucleosis phenotype and concurrently, 17 subjects of this group had aplastic anemia. All subjects with aplastic anemia died within a wk. Aplastic anemia did not accompany hypogammaglobulinemia or malignant lymphoma phenotypes. Hypogammaglobulinemia had been detected before infectious mononucleosis in there subjects, after infectious mononucleosis in five subjects, and was not associated with infectious mononucleosis in 11 boys with hypogammaglobulinemia. In nine subjects infectious mononucleosis appeared to have evolved into malignant lymphoma; however, the majority of patients with malignant lymphoma showed no obvious antecedent infectious mononucleosis. One subject had infectious mononucleosis following recurrent malignant lymphoma. Twenty-six of 35 lymphomas were in the terminal ileum. Results of immunologic and virologic studies of 15 survivors revealed combined variable immunodeficiency and deficient antibody responses to EBV-specific antigens. Mothers of boys with XLP exhibited abnormally elevated titers of antibodies to EBV. Subjects of both sexes with phenotypes of XLP should be investigated for immunodeficiency to EBV. Persons with inherited or acquired immunodeficiency may be vulnerable to life-threatening EBV-induced diseases. (Author abstract) (26 Refs)

ANTITUMOR ACTIVITY AND IMMUNOTHERAPY

25. HETEROGENEITY OF HUMAN MELANOMA-ASSOCIATED ANTIGENS DEFINED BY MONOCLONAL ANTIBODIES AND CONVENTIONAL XENOANTISERA.

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Cancer Immunol Immunother; 13(1):69-74 1982

Types of 94,000 (94K) dalton and high-mol-wt antigens synthesized by cultured melanoma cells were studied. The monoclonal antibodies (MoAb) 376.96S, and 465.12S, and the polyclonal xenoantisera 8823 and 8986 all immunoprecipitated structures which when electrophoresed under reducing conditions gave apparent molecular weights of 94K. Sodium dodecyl sulfate polyacrylamide gel electrophoresis under nonreducing conditions showed that the 94K dalton molecules detected by the xenoantiserum 8823 exhibited a decrease in apparent mol wt to 82K daltons, while the structures identified by MoAb 465.12S, 376.96S, and xenoantiserum 8986 showed a decrease in apparent mol wt to 86K daltons. The MoAb 376.96S occasionally detected a small amount of 94K component in the spent medium of cultured melanoma cells, the xenoantiserum 8823 reacted with fibronectin while the MoAb 465.12 and xenoantiserum 8986 immunoprecipitated a major 94K and a minor 72K dalton structure. Immunodepletion experiments showed that the MoAb 465.12 and the xenoantiserum 8986 each reacts with the same population of 94K dalton molecules present in the spent medium of 3H-glucosamine-labeled melanoma cells. MoAb 225.28S and the xenoantiserum 8995 both immunoprecipitated two components from 3H-glucosamine-labeled melanoma cells BwV. Data indicated that the antigenic determinant detected by the MoAb 225.28S is not present on all the molecules comprising the 280K and greater than 440K dalton high-mol-wt melanoma-associated antigen system. (24 Refs)

26. EFFECTS OF ANTIBODIES TO CHORIOGONADOTROPIN IN MALIGNANT GROWTH. II. SOLID TRANSPLANTABLE RAT TUMORS.

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Cancer Immunol Immunother; 13(1):2-4 1982

Effects of preimmunization against choriogonadotropin (CG) were studied in two transplantable solid neoplasms, the R 3230 AC rat mammary adenocarcinoma and the 5123 1-1 rat hepatoma which have been shown to synthesize CG-like material. R 3230 AC rat mammary adenocarcinoma was maintained in Fischer 344 female rats, and the 5123 1-1 rat hepatoma was maintained in Buffalo female rats. A conjugate of the beta-subunit of CG and tetanus toxoid (CGb-tt) was used for immunization and induction of CG antibodies. An av of 1.30 ug of the immunogen was injected sc in the interscapular area on days 0, 7, and 14; after the last injection, 14 days were allowed for optimization of the antibody production before implantation of the respective tumor. One of two con control groups was administered purified tetanus toxoid, approx 0.7 ug/injection, following the same schedule as with CGb-tt, while the other received saline only. After sacrifice, serum was tested for anti-CG antibodies with the use of the hCG-beta-RIA kit. The two control groups did not show any binding of 125I-hCG, while all animals immunized against CG had a significant titer of CG antibodies. Induction of anti-CG antibodies induced a significant reduction of tumor mass in all preimmunized animals for both tumor models. Tumor take after implant of 10 mg Stadie slices, however, was not prevented by preimmunization. Histopathology and growth pattern of the tumors were identical in all groups. Results demonstrated that immunization against CG has a definitive biological effect in transplantable solid tumors by significantly retarding the growth of the two tumor models. (16 Refs)

27. EXPRESSION OF NEUROECTODERMAL ANTIGENS COMMON TO MELANOMAS, GLIOMAS, AND NEUROBLASTOMAS. I. IDENTIFICATION BY MONOCLONAL ANTI-MELANOMA AND ANTI-GLIOMA ANTIBODIES.

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Acta Neuropathol (Berl); 57(2/3):158-164 1982

In studies in mice, the reactivity spectrum of five monoclonal anti-melanoma antibodies (Ab; Mel-5, Mel-14, Me3-TB7, Me4-F8, Me5-D5) cross-reacting with gliomas and neuroblastomas and one monoclonal anti-glioma Ab was determined in an Ab-binding radioimmunoassay. Ab from Me5 bound to 5/7 gliomas and to 3/3 neuroblastomas. Ab from Mel-14 also bound to 5/7 gliomas but to only one neuroblastoma. Similar, but not identical cross-reactivities, occurred with the other anti-melanoma clones. None of the anti-melanoma clones reacted with 33 non-melanoma control cell lines. The monoclonal anti-glioma Ab, G13-C6, bound to 8/9 melanoma cell lines and to 1/3 neuroblastoma lines. Results of the study indicated that the antigenic determinants detected by these Ab were not associated with the same antigen, thus suggesting the existence of at least six different antigens common to melanomas, gliomas, and neuroblastomas. While all the tumors studied are derived embryologically from the neural crest, absorption with homogenate of a whole brain of a fetus at 20 wk of gestation abolished only the binding of monoclonal anti-glioma antibody, but did not modify the binding of monoclonal anti-melanoma Ab. (16 Refs)

28. THE IMMUNOHISTOCHEMICAL REACTIVITY OF A HUMAN MONOCLONAL ANTIBODY WITH TISSUE SECTIONS OF HUMAN MAMMARY TUMORS.

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Cancer; 50(2):241-249 1982

Human monoclonal antibodies have been generated following the fusion of human lymphocytes (obtained from axillary lymph nodes of mastectomy patients) with a murine nonimmunoglobulin secreting myeloma cell line. We report a detailed analysis of the reactivity of a human IgM monoclonal antibody secreted by one of these double cloned hybridoma cell lines. Tissue sections of both malignant and benign human mammary tumors, as well as apparently normal tissues, were tested using the immunoperoxidase technique and the human monoclonal antibody. Eighty-one per cent (54/67) of primary malignant mammary tumors, 100% (20/20) of metastatic breast lesions, and 14% (3/22) of benign breast lesions reacted positively with a moderate or strong intensity. The per cent of mammary carcinoma cells that stained and the pattern of staining varied among different tumor samples. While reactivity was observed with selected carcinomas of nonbreast origin, little or no reactivity was observed with apparently normal human tissues including normal mammary epithelium. The antibody reactivity observed was shown to be clearly distinct from those of both anti-T and anticarcinoembryonic antigen sera. (Author abstract) (19 Refs)

29. REGRESSION OF CANINE MAMMARY CARCINOMA AFTER IMMUNOADSORPTION THERAPY.

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Cancer Res; 42(9):3663-3668 1982

The plasma of dogs afflicted with mammary carcinoma was perfused through chambers bearing Staphylococcus aureus Cowan Strain 1 in an attempt to remove tumor-promoting, immunosuppressive immune complexes from the peripheral blood of these animals. In this canine model of spontaneous mammary carcinoma, reduction of breast and/or soft-tissue tumor (posttreatment size equal to 0 to 50% of pretreatment tumor size) was observed in 5 of the 10 animals so treated. Immune complexes capable of blocking lymphocytotoxicity were measured pre- and postimmunoadsorption; removal was more efficient in the five responders (4 of 6 complexes) than in nonresponders (1 of 10 complexes), although statistical significance was not attained. The reduction of tumor size seen in soft-tissue sites was not always accompanied by a similar reduction of tumor size in visceral sites, and surgical resection of residual soft-tissue tumor nodules remaining after immunoadsorption treatment was required to achieve a complete response in two responding animals. No significant decrease in tumor size was observed in the control group, perfused without immunoadsorbent, nor in five additional tumor-bearing animals infused with normal dog plasma which had been passed through S aureus Cowan Strain 1-containing chambers. These data indicate that immunoadsorption of tumor-bearing host plasma can result in reduction in size of canine mammary adenocarcinoma but that the response is dependent on the site of the tumor (sc versus visceral) and may require utilization of other modalities to achieve a complete disappearance of the tumor. (Author abstract) (31 Refs)

30. EXPRESSION ON CULTURED HUMAN TUMOUR CELLS OF PLACENTAL TROPHOBLAST MEMBRANE ANTIGENS AND PLACENTAL ALKALINE PHOSPHATASE DEFINED BY MONOCLONAL ANTIBODIES.

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Int J Cancer; 30(1):21-26 1982

The cellular reactivity of six monoclonal antibodies (McAbs) produced to isolated human placental syncytiotrophoblast microviilous plasma membranes has been examined using a variety of normal and malignant cell types. Two McAbs reacted with antigenic determinants common to most normal human cells. Two other McAbs (H310 and H316) reacted predominantly with normal placental trophoblast and with lymphocytic cells, as well as with most transformed or neoplastic cultured cell lines. Two further McAbs (H315 and H317) identified fetal differentiation antigens expressed only on the membranes of normal placental trophoblast and of certain tumor cell lines. H317 has been shown to be specific for the heat-stable L-phenylalanine-inhibitable placental-type alkaline phosphatase isoenzyme. These latter McAbs (H315 and H317) may prove useful in monitoring of some human cancers. (Author abstract) (36 Refs)

31. SEROLOGICAL ANALYSIS OF CELL SURFACE ANTIGENS OF NULL CELL ACUTE LYMPHOCYTIC LEUKEMIA BY MOUSE MONOCLONAL ANTIBODIES.

Ueda R, Tanimoto M, Takahashi T, Ogata SI, Nishida K, Namikawa R, Nishizuka Y, Ota K
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Proc Natl Acad Sci USA; 79(14,part1):4386-4390 1982

Nine antigen systems were defined. Two were related to HLA-A,B,C and to Ia-like antigens; the others could be grouped into three categories. (i) NL-22, NL-1: NL-22 antibody reacted with leukemia cells from 12 of 16 cases of null cell acute lymphocytic leukemia (null-ALL) but not with any other type of leukemia tested or with lymphoid cells of various origins. Among cultured cell lines tested, one (NALM-6) of three null-ALL cell lines was positive; the others were negative. Absorption analysis confirmed the restriction of NL-22 antigen to null-ALL. NL-1 antibody was reactive with leukemia cells from 10 of 16 cases of null-ALL and 3 of 6 cases of chronic myelocytic leukemia in blastic crisis (CML-BC). The antigen was present also on a minor population of normal lymphoid cells. The distribution and mol wt (100,000; glycoprotein) of the NL-1 antigen resembled that of the previously described common ALL antigen (cALL). (ii) NL-30, NL-4: Both antibodies exhibited almost identical patterns of reactivities against cultured cell lines tested. They reacted with leukemia cells from some cases of null-ALL, adult T-cell leukemia, and CML-BC, although they showed discordance in their reactivities against a panel of leukemia cells. (iii) NL-9, NL-8, NL-25: These three antibodies detect serologically distinguishable determinants on a broad range of leukemias and normal lymphoid and hematopoietic cell types. The antibodies analyzed in this study provide evidence for the heterogeneity of null-ALL by demonstrating a variety of antigen phenotypes on leukemia cells. One of the antigens (NL-22) appears to be restricted to null-ALL. (Author abstract) (27 Refs)

32. IMMUNOCHEMICAL CHARACTERIZATION OF PROSTATIC ACID PHOSPHATASE WITH MONOCLONAL ANTIBODIES.

Lee CL, Li CY, Jou YH, Murphy GP, Chu TM
Roswell Park Memorial Inst., Buffalo, NY, 14263
Ann NY Acad Sci; 390:52-61 1982

Hybridoma-derived monoclonal antibodies to human PAP have been produced by fusion of mouse myeloma cells (P3x63 Ag8.653) with spleen cells from mice immunized with purified PAP. One hundred fifty-six out of 252 clones were found to produce antibodies against PAP. These monoclonal antibodies were classified into four different subclasses as IgM (3 clones), IgG2a (2 clones), IgG3 (1 clone), and IgG1 (150 clones) with k-chains. Four monoclonal antibodies. IgG1, IgG2a, IgG3, and IgM, were selected from the 156 hybridoma clones for immunologic characterization. Results from a binding assay suggested that monoclonal anti-PAP antibodies IgG1 and IgM recognized two distinct antigenic determinants of the PAP molecule, while the hybridoma IgG2a and IgG3 antibodies recognized another antigenic determinant. The specificity of these four hybridoma anti-PAP antibodies has been evaluated by the immunohistochemical method and competitive-binding assay. Monoclonal antibodies IgG2a and IgG3 as well as polyclonal xenoantibodies were found to react with PAP as well as with nonprostatic acid phosphatases; and antibodies IgG1 and IgM reacted more specifically with PAP. These results indicated that monoclonal anti-PAP antibodies IgG1 and IgM possessed a higher specificity for human PAP in comparison with monoclonal antibodies IgG2a, IgG3, and xenoantibodies. The monoclonal anti-PAP IgG1 and IgM antibodies may be useful in delineating antigenic structure of the PAP molecule, as well as in the refinement of serologic determination and immunocytochemical study of PAP in human prostate cancer. (Author abstract) (22 Refs)

33. THE IMMUNOLOGICAL CLASSIFICATION OF LEUKAEMIA BASED ON A RAPID MICROCYTOTOXICITY TEST.

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Clin Exp Immunol; 49(1):142-148 1982

We describe a rapid, accurate, and reproducible cytotoxic antibody test for the immunological classification of leukemia. Well characterized heteroantisera and monoclonal antibodies were distributed in a microcytotoxicity tray referred to as a leukemia screening tray (LST). Leukemia cells were tested for the presence of Ia-like, 'blast', thymocyte, common acute lymphoblastic leukemia (cALL), and acute myeloblastic leukemia (AML) antigens. Utilizing this technique, T ALL could be distinguished from non-T ALL, ALL and AML could be differentiated, the myeloid blast crisis of chronic myelogenous leukemia (CML) could be distinguished from the lymphoid blast crisis, and the T lymphocyte and B lymphocyte lymphoid leukemias were readily identified. It has been shown that subclassification of leukemia according to surface markers, as described here, offers considerable improvement in the diagnosis and treatment of leukemia over the classical morphological methodologies. Because the test can be completed in 2 hr and unlimited amounts of monoclonal antibodies are available, the LST or similar tests should become universally available in the future to supplement morphological data and replace other lengthy enzyme and rosetting tests. (Author abstract) (34 Refs)

34. STUDIES ON THE CLONAL ORIGIN OF HUMAN B CELL LEUKEMIA USING MONOCLONAL ANTI-IDIOTYPE ANTIBODIES.

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J Immunol; 129(2):904-910 1982

The clonal origin of an IgA1kappa B cell leukemia in a 71-yr-old man (WF) was examined using a monoclonal anti-Id antibody and a panel of monoclonal anti-VH antibodies. Immunofluorescent studies revealed that all surface IgA1kappa+ leukemic cells in WF's blood and 10% of the IgM+ B cells in his bone marrow expressed the WF Id. Three percent of the IgA1kappa+ leukemic cells in blood also expressed gamma-chains in their cytoplasm. Approximately 0.1%, 1%, and 10% of bone marrow mononuclear cells, respectively, expressed u-chains, gamma-chains, and alpha-chains in their cytoplasm, but no detectable light chains or surface immunoglobulins. These u-, gamma-, and alpha-positive cells had the convoluted nucleus and narrow cytoplasm characteristic of normal u+ pre-B cells. Sequential isotype switching among this unusual pre-B population was indicated by co-expression of u-chains and alpha-chains by 11% and 63%, respectively, of the gamma pre-B cells. These pre-B cells and the surface alpha-chains and cytoplasmic gamma-chains of the leukemic B cells were reactive with one of four monoclonal anti-VH antibodies. The data suggest malignant transformation of the clone before isotype switching, and also imply light chain precommitment at the pre-B cell level of differentiation. (Author abstract) (35 Refs)

35. CELL SURFACE ANTIGEN PHENOTYPES AND ENZYME EXPRESSION PATTERNS OF TWO MURINE T-CELL LYMPHOMAS DERIVED FROM EARLY AND/OR MATURE THYMUS CELLS.

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Leuk Res; 6(3):425-428 1982

Expression of cell surface antigens on SL2 and GRSL13 cells and enzyme cytochemistry of murine SL2 and GRSL13 lymphoma cells were investigated. SL2 lymphoma occurred as a spontaneous tumor in DBA/2 mice, and GRSL13 lymphoma occurred as a spontaneous lymphoma in GRS mice. While T200 antigen expression was high on both lymphomas, Thy1 was low on GRSL13 and high on SL2. Significant difference between the two lymphomas was obtained using antibodies 30-G12 (anti-T200) and 30-H11 (anti-glycolipid) with positivity on GRSL13 and no reaction on SL2; a reverse pattern was seen with antibodies 53-7.3 (anti-Lyt1) and 53-6.7 (anti-Lyt2). Since ThB and the glycolipid detected by antibody 30-H11 were expressed on bone marrow cells and since ThB was not expressed at all on peripheral T cells, the antigens are apparently characteristic for the more primitive cells in the thymic series. Results showed that GRSL13 represents a T cell of a more primitive immature type, while SL2 represents a more mature T cell. Enzymes present and clearly expressed in the lymphomas as well as the majority of thymus cells were acid phosphatase, beta-glucuronidase, non-specific esterase, and alphanaphthyl-acetate-esterase. No clear difference was observed between the two lymphomas and the normal thymus cells. (17 Refs)

36. PROBING HUMAN MALIGNANT T CELLS WITH LECTINS: A COMPARISON WITH THEIR SURFACE ANTIGEN PATTERNS DEFINED BY MONOCLONAL ANTIBODIES.

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Leuk Res; 6(3):307-312 1982

Tumor populations (TP) of 53 patients (40 children, 13 adults) with T cell malignancies were investigated with lectins and the lectin- and monoclonal antibodies-defined phenotypes were compared. Fifteen patients had TP resembling early thymocytes (T6-, T3-phenotype): 2 had peanut agglutinin positive (PNA+) and soybean agglutinin positive (SBA+) malignant cells (1 child with lymphoblastic lymphoma, 1 adult with acute lymphoblastic leukemia), and 13 had PNA-negative (PNA-) and SBA-negative (SBA-) malignant cells. Among the patients with T6+, T3-tumor cell populations resembling corticothymocytes (15 children, 1 adult), five had PNA-, SBA- malignant T cells; three PNA+, SBA+; seven PNA+, SBA-; and one PNA-, SBA+ malignant T cells. Six patients (5 children, 1 adult) had cells displaying both T6 and T3 antigens. Three of the six patients had PNA+, SBA- cells; two PNA-, SBA+; and one PNA-, SBA- cells. Among 16 patients (6 children, 10 adults) with T6-, T3+ malignant cells, 13 had PNA-, SBA- cells, thus resembling peripheral T cells. Three of 16 patient with T6-, T3+ cells had PNA-, SBA+ cells. These cell populations can be related to medullary thymocytes rather than peripheral T cells. The results showed that in spite of a high degree of heterogeneity of malignant T cell populations in the pattern of surface antigens, the populations appear to conform essentially to the scheme of normal T cell differentiation. (28 Refs)

37. ANALYSIS OF HUMAN LEUKEMIA/LYMPHOMA CELL LINES WITH MONOCLONAL ANTIBODIES BA-1, BA-2 AND BA-3.

LeBien T, Kersey J, Nakazawa S, Minato K, Minowada J
Dept. Lab. Medicine and Pathology, Univ. Minnesota, Box 609 Mayo, Minneapolis, MN, 55455
Leuk Res; 6(3):299-305 1982

Results of testing 67 human leukemia/lymphoma cell lines with monoclonal antibodies BA-1, BA-2, and BA-3 are reported. Monoclonal antibody BA-1 showed less than 20% binding to any of 20 T acute lymphoblastic leukemia (ALL) cell lines. Approx 15% of MOLT-10 cells were BA-1 positive when tested on several occasions. Analysis of the other 19 cell lines with BA-1 consistently gave 0% reactivity using direct immunofluorescence. Both BA-2 and BA-3 showed significant binding to 7/20 and 7/20 T ALL lines, respectively. Very little overlap in the reactivity of BA-2 and BA-3 with T ALL cell lines was observed; only RPMI-8402 and MOLT-10 reacted with both antibodies. Sixteen non-T ALL cell lines included both pre-B (cytoplasmic IgM+, surface Ig-) and non-pre-B (cytoplasmic IgM-, surface Ig-). With one exception the three antibodies reacted with all cell lines tested. In most instances greater than 90% of cells from a given cell line were strongly reactive with BA-1, BA-2, and BA-3. Twenty-four cell lines were established from patients with B ALL, non-Hodgkin's lymphoma, and Burkitt's lymphoma. All cell lines expressed varying amounts of surface Ig. BA-1 bound to 15 cell lines, BA-2 to 9, and BA-3 to 17 cell lines. No correlation was observed between antibody reactivity and expression of a particularly heavy or light chain class. Ba-1, BA-2, and BA-3 were assayed against seven leukemic cell lines of myeloid/monocytoid origin. BA-1 showed partial reactivity with the K-526 cell line, whereas BA-2 was reactive with most K-526 cells. BA-3 did not bind any of the seven cell lines. Thus, BA-1,-2, and-3 bind primarily, but not exclusively, to leukemias of B-cell lineage. (31 Refs)

38. EVALUATION OF A TISSUE TRANSPORT MEDIUM FOR IMMUNOLOGICAL CHARACTERIZATION OF BENIGN AND MALIGNANT LYMPHOID TISSUES.

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Am J Clin Pathol; 78(1):8-13 1982

A tissue transport medium was evaluated for its usefulness in immunologic characterization of lymphocytes in tissue sections. A variety of lymphoid tissues were studied, including normal tissue, hyperplastic tissue and malignant lymphoma. Approximately equal parts of biopsy samples were taken and one part was immediately snap-frozen while the other was held in transport medium for up to 1 week before processing for frozen section. Sections were stained with fluorescein-conjugated anti-immunoglobulin antisera and with a variety of murine monoclonal antibodies to T-cell antigens or Ia antigen followed by staining with fluorescein-conjugated goat-antimouse gamma globulin. In all cases studied, there was complete agreement in the staining patterns of tissues which were either immediately snap-frozen or held in transport medium. (Author abstract) (19 Refs)

IMMUNOGLOBULIN STRUCTURE AND SYNTHESIS

39. THE INTERACTION OF MOUSE MYELOMA IMMUNOGLOBULIN S15 WITH NEGATIVELY CHARGED POLYSACCHARIDE ANTIGENS.

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Mol Immunol; 19(7):913-923 1982

A murine BALB/c IgG2a (lambda3) myeloma immunoglobulin SAPC-15 with binding activity for negatively charged polysaccharides has been purified by affinity chromatography, and its interaction with heparin and various other polyanionic antigens has been studied. The antigen-binding activity has been demonstrated to reside in the Fab part of the immunoglobulin. The S15 myeloma protein in 0.05 M Tris buffer at pH 7.4 precipitated dextran sulfate, heparin, chondroitin sulfate A, B and C, hyaluronic acid, H influenzae Type b polysaccharide, calf thymus DNA, Klebsiella polysaccharide K63 and poly-L-glutamic acid. Of these antigens only dextran sulfate was precipitated in 0.01 M phosphate buffered saline (0.15 M), pH 7.4. The pepsin S15 Fab fragment did not precipitate with any of these antigens. The intrinsic tryptophanyl fluorescence of S15 was changed maximally by the addition of heparin, and the binding affinity of the immunoglobulin for this antigen was high (greater than 10(6) L/M). S15 may resemble antibody molecules that react with antigens under non-physiological conditions or in pathological conditions or in the external environment as in the lumen of the gut. All the above interactions of S15 with antigens persisted in 0.05 M Tris buffer made physiologically isotonic by the addition of sucrose, and S15 could thus be used to identify these antigens on cell surfaces. (Author abstract) (49 Refs)

40. THE EFFECT OF ANTI-IA ANTIBODY ON IMMUNOGLOBULIN-SECRETING CELLS FROM HEALTHY INDIVIDUALS AND MYELOMA PATIENTS.

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Scand J Immunol; 15(6):567-571 1982

Immunoglobulin-secreting cells (ISC) in the peripheral blood of healthy individuals and in the bone marrow, peripheral blood, or plasmacytomas of patients with multiple myeloma were enumerated by a protein-A plaque-forming cell assay after treatment with anti-Ia antibody and complement. Rabbit anti-human B-cell antisera and monoclonal anti-Ia antibody (OKIal) were used. By this treatment, the number of ISC in the peripheral blood of healthy individuals decreased to half, and that of M-protein-secreting cells from some patients with multiple myeloma also decreased markedly. In one patient, the number of M-protein-secreting cells in the bone marrow were markedly reduced by this treatment, but this was not the case after 6 mo of chemotherapy, suggesting that the chemotherapy reduced chiefly the Ia-positive myeloma cells rather than Ia-negative myeloma cells. (Author abstract) (15 Refs)

41. DIFFERENCES IN THE NUCLEASE SENSITIVITY BETWEEN THE TWO ALLELES OF THE IMMUNOGLOBULIN KAPPA LIGHT CHAIN GENES IN MOUSE LIVER AND MYELOMA NUCLEI.

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Nucleic Acids Res; 10(12):3627-3645 1982

In mouse myeloma T the productive kappa light chain gene differs from its aberrantly rearranged allele in the patterns of DNAase I hypersensitive sites. In the region of the alleles where they are identical in sequence they have one site in common which lies 0.8 kb downstream of the coding region; but two sites upstream of and within the C gene segment (2) are found only on the non-productive allele. Within the region of different sequences both alleles have analogously located DNAase I hypersensitive sites; they lie 0.15 kb upstream of the respective leader segments and cover putative promoter sequences. Only one of the six DNAase I hypersensitive sites is also very sensitive towards micrococcal nuclease due to its particular DNA sequence. The non-rearranged gene studied in liver nuclei has no DNAase I hypersensitive sites but is preferentially cleaved in A/T rich regions. (Author abstract) (35 Refs)

42. A PHORBOL ESTER TUMOR PROMOTER INDUCES CHANGES IN THE EXPRESSION OF IMMUNOGLOBULINS AND DR ANTIGENS IN HUMAN LYMPHOBLASTOID CELLS.

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J Immunol; 129(2):539-544 1982

The present study indicates that 12-O-tetradecanoyl phorbol 13-acetate (TPA) can induce either increases or decreases in the relative expression of membrane-associated IgM and IgD as well as the expression of other markers of lymphocyte differentiation on human B lymphoblasts, depending on the clone studied. The changes in membrane Ig expression are apparent within 24 hr and are maximal at about 48 hr after the addition of the compound. In clone BL, TPA decreases the membrane IgM/IgD ratio as determined by the percentage of cells bearing these isotypes and by their densities on single cells. In clone MW-E, TPA has the opposite effect. Although these changes are followed by an increase in Ig secretion by MW-E cells, measured by immunofluorescence and the protein A plaque assay, There is no induction of Ig secretion in BL cells. In addition, TPA increases the expression in BL of an additional B lymphocyte marker, the D region-related (DR) antigens, while having the opposite effect in MW-E. In two sublines of Daudi, a membrane IgM-positive, IgD-negative, nonsecreting cell line, TPA treatment resulted in the expression of membrane IgD without the induction of Ig secretion. Thus, the TPA-induced changes in the IgM/IgD ratio and Dr antigen expression are inversely related and are not due to differential proliferation of subpopulations. Taken together, it appears that, depending on the particular clone of B lymphoblasts studied, TPA can induce or inhibit a coherent program of B lymphocyte maturation. (Author abstract) (52 Refs)

43. EFFECTS OF IMMUNOGLOBULIN STRUCTURE ON FC RECEPTOR BINDING: A MOUSE MYELOMA VARIANT IMMUNOGLOBULIN WITH A GAMMA2B-GAMMA2A HYBRID HEAVY CHAIN HAVING A COMPLETE GAMMA2A FC REGION FAILS TO BIND TO GAMMA2A FC RECEPTORS ON MOUSE MACROPHAGES.

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Dept. Cell Biology, Albert Einstein Coll. Medicine, Bronx, NY, 10461

J Immunol; 129(2):610-614 1982

We report here the primary structure of an immunoglobulin heavy chain synthesized by ICR 16, a variant of the MPC 11 mouse myeloma cell line. The ICR 16 heavy chain is a gamma2b-gamma2a hybrid, consisting of the CH1 domain of gamma2b and the hinge, CH2, and CH3 domains of gamma2a subclasses. The genetic mechanism by which ICR 16 occurred may be recombination, based on homologies in both coding and intervening sequences in gamma2b and gamma2a constant region genes. Although the Fc fragment of ICR 16 is completely gamma2a-like and has been shown to bind to gamma2a Fc receptors on mouse macrophages, the intact H2L2 molecule is unable to do so. Such an observation underscores the crucial role that conformation may play in the ability of immunoglobulins to carry out biologic functions. (Author abstract) (41 Refs)

44. SOMATIC VARIANTS OF MURINE IMMUNOGLOBULIN LAMBDA LIGHT CHAINS.

Bothwell AL, Paskind M, Reth M, Imanishi-Kari T, Rajewsky K, Baltimore D

Center for Cancer Res., Massachusetts Inst. Technology, Cambridge, MA, 02139

Nature; 298(5872):380-382 1982

The nucleotide sequences of lambda complementary DNA clones, two lambda 1 genes from hybridomas and a lambda 2 gene from a myeloma, were determined. It was demonstrated that somatic mutations in lambda chains do not have to be localized in the complementarity-determining regions (CDR), as they can occur in both the framework and the CDR residues. (25 Refs)

45. DEMONSTRATION OF IMMUNOGLOBULIN IN MALIGNANT LYMPHOMAS. USE OF AN IMMUNOPEROXIDASE TECHNIC ON FROZEN SECTIONS.

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Immunopathology Unit, Massachusetts General Hosp., Boston, MA, 02114

Am J Clin Pathol; 78(1):14-21 1982

We used an immunoperoxidase technic to detect surface and cytoplasmic immunoglobulin in frozen sections of 46 malignant lymphomas. With the immunoperoxidase technic, differential staining with antisera to the various heavy and light chain classes permitted detection and characterization of monotypic immunoglobulin in frozen sections of 15 of 15 nodular lymphomas and 24 of 31 diffuse lymphomas. The immunoperoxidase technic applied to frozen sections is a convenient and reliable method for the detection of immunoglobulin in lymphoid tissues, which can be performed in a pathology laboratory without the need for special equipment. (Author abstract) (28 Refs)

46. DIFFUSE FOLLICULAR LYMPHOID HYPERPLASIA OF THE SMALL INTESTINE WITHOUT PRIMARY IMMUNOGLOBULIN DEFICIENCY.

Rambaud JC, De Saint-Louvent P, Marti R, Galian A, Mason DY, Wassef M, Light H, Valleur P, Bernier JJ

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Am J Med; 73(1):125-132 1982

Three cases of follicular lymphoid hyperplasia extending to the whole length of the small intestine are reported in three young adult patients of low economic status. The disease was revealed by chronic diarrhea with malabsorption and/or protein-losing enteropathy. In one patient, all transitional patterns were found between the hyperplastic follicles and a small intestinal multicentric centrocytic-centroblastic lymphoma. No abnormalities in humoral or cellular immunity were found in the three patients. In particular, serum immunoglobulins (except IgG in one case) and plasma cell populations of small intestinal lamina propria were normal. Diffuse follicular lymphoid hyperplasia of the small intestine in the absence of primary immunoglobulin deficiency appears to be a rare condition associated with (or leading to) intestinal malignant lymphoma in most cases. Patients usually belong to the same populations as those suffering from alpha-chain disease. (Author abstract) (34 Refs)

HUMORAL IMMUNE BLOCKING FACTORS AND ANTIGEN-ANTIBODY COMPLEXES

47. CIRCULATING IMMUNE COMPLEXES, ANTIGENS, AND ANTIBODIES RELATED TO THE MURINE MAMMARY TUMOR VIRUS IN C3H MICE.

Dong ZW, Witkin SS, Fernandes G, Sarkar NH, Good RA, Day NK (c/o Day), Oklahoma Medical Res. Foundation, 825 N.E. 13th St., Oklahoma City, OK, 73104
J Immunol; 129(2):872-876 1982

A comparative study was performed to measure levels of free antibody to MuMTV, MuMTV membrane antigen (gp52), and antigen-antibody complexes in sera of mammary tumor-bearing and age-matched non-tumor bearing C3H/Bi mice. Approx 90% of these mice spontaneously develop breast cancer. Levels of MuMTV antibody and C3-containing circulating immune complexes (CIC) were highest in the sera of the mice without overt evidence of breast cancer. MuMTV gp52 antigen was present in higher concentrations in the sera of mice with overt breast cancer. Fractionation of the sera on sucrose gradients followed by analysis for CIC confirmed that levels of C-containing CIC were lower in sera from mice with tumors than in nontumor bearers. The CIC were, however, of smaller size in sera of tumor-bearing mice. When the sera were assayed for CIC by an assay in which C binding does not compete with binding of CIC to the sperm, the levels of these small-sized CIC in sera of mice with breast cancer were now comparable to CIC levels in nontumor-bearing mice. MuMTV antibody was located in both 7S and high mw regions of the gradients. To determine whether the CIC contained MuMTV antigen, the CIC were bound to bull sperm Fc receptors and assayed for reactivity with monospecific goat anti-gp521gG. Significantly higher levels of reactivity to anti-gp52 were detected in CIC from C3H mice than in CIC from sera of age-matched AKR mice with or without leukemia or from MRL/MpJ-Ipr/Ipr mice. These data indicate that there is a shift from MuMTV antibody excess to MuMTV antigen excess and from larger C-fixing CIC to smaller non-C-fixing CIC after appearance of overt breast cancer in C3H mice. (26 Refs)

48. IDENTIFICATION OF THE PLATELET ALLOANTIGEN (PI[A1]) IN CIRCULATING IMMUNE COMPLEXES OF NORMAL HUMAN SERA.

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Cancer Immunol Immunother; 13(1):44-47 1982

Cell membrane fragments associated with polyethylene glycol (PEG) precipitates were examined to find out whether the fragments represent remnants of platelet membranes. The PI[A1] alloantigen present on platelets was used as antigenic marker for identification of platelet fragments. Unabsorbed anti-PI[A1] serum gave positive results at a dilution of 1/16-1/8. The inhibition of the reaction of anti-PI[A1] serum with PI[A1]-positive platelets was proportional to the amount of circulating immune complexes (CIC) incubated with the anti-PI[A1] before the immunofluorescence test. Anti-PI[A1] serum induced 89% of the maximum platelet lysis. Prior incubation of antisera with CIC inhibited lysis which was proportional to the amount of CIC added: there was 100% inhibition with 940 ug and 50% inhibition with 470 ug. Anti-PI[A1] serum was used undiluted or diluted in parallel experiments. A one-half dilution of the serum induced 68% of maximum lysis. Complete inhibition was observed with 470 ug CIC when the anti-PI[A1] was used at this dilution. The percent inhibition of chromium lysis by CIC was not significantly modified when the platelets were treated with bromelain. Results of the inhibition of immunofluorescence and of the inhibition of chromium lysis assays indicated that material reacting with anti-PI[A1] antibodies is present in 3.5% PEG precipitates of normal human sera and that some of the cell fragments in CIC could represent platelet membrane. (19 Refs)

49. CIRCULATING IMMUNE COMPLEXES DETECTED BY BINDING OF RADIOLABELLED PROTEIN A IN PATIENTS WITH ORAL CANCER AND ORAL PREMALIGNANT LESIONS.

Scully C, Barkas T, Boyle P, McGregor IA
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J Clin Lab Immunol; 8(2):113-115 1982

Serum immune complexes and immunoglobulins were examined in 48 Caucasian patients with histologically confirmed squamous cell carcinoma, 17 with oral keratosis and variable degrees of epithelial dysplasia (leukoplakia), and 49 controls matched as closely as possible for age and sex. Circulating levels of immune complexes (expressed as ug equivalents aggregated IgG/ml) were significantly higher in patients with oral cancer, median 33, than in controls, 13, but not significantly higher than in patients with oral keratosis, 22. No correlation could be determined between serum levels of immune complexes and the clinical stage in patients with oral cancer. (30 Refs)

HUMORAL IMMUNOSUPPRESSIVE AGENTS

50. SELECTIVE ACTION OF ALKYLATING AGENTS AGAINST CELLS PARTICIPATING IN SUPPRESSION OF ANTIBODY RESPONSES.

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Int J Immunopharmacol; 4(3):159-166 1982

The effect of several alkylating agents of known immunosuppressive potential on suppressor cells which are effective in a secondary host was investigated. Supraoptimal immunization (SOI) (ip injection of 4 X 10(9) SRBC into 8-10-wk-old (C57/B1 X DBA2)F1 (BDF1) mice) induced suppressor cells which were sensitive to anti-thymocyte serum and complement. None of the alkylating agents injected 2 days prior to SOI prevented the induction of suppressor cell effectors capable of exerting suppression in the secondary host. When injected 2 days following SOI, both cyclophosphamide (CP) and carmustine (BCNU) caused a dramatic reduction in the capability of donor splenocytes to induce suppression in the secondary host. CP and BCNU, but not lomustine, semustine, and melphalan, when injected 2 days after SOI, severely curtailed the expression of suppressor activity when transferred on day 14. T suppressor effector cells were more sensitive to CP than to BCNU. As suppressor cells differentiated and matured after SOI, their sensitivity to CP gradually diminished. These results indicate that equally potent immunosuppressive agents can have diverse effects on the induction and expression of suppressor cells and their action may depend on time of administration in relation to antigen. (30 Refs)

51. THE MECHANISM OF TUMOR ALLOGRAFT SURVIVAL INDUCED BY CP-17,193.

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Immunopharmacology; 4(4):341-354 1982

A novel immunosuppressive, 2-(4'-chlorophenyl)benzothiopyrano-(4,3-c)pyrazolo-3 one (CP-17,193) was examined for its immunosuppressive effects in vivo and for its promotion of El4 tumor allograft survival. Balb/c mice received 1 x 10(7) El4 tumor cells ip on day 0, then were dosed with 10 mg/kg po of either CP-17,193 or cyclophosphamide (CYC) or placebo on days 0, 1, 3, 4, 5, 6, 7, and 8. Both drugs showed near complete suppression of the immune response on day 10 and good tumor graft survival. Subsequently, the humoral immune response to CP-17,193 rose toward and overshot the control titer by day 17, then slowly fell back to control levels. Antibody titers to CYC remained suppressed through day 17. Discontinuation of CYC resulted in prompt restoration of cellular cytotoxicity by day 17, while after CP-17,193 treatment, normalization of cellular cytotoxicity followed a more protracted course, and was effectively complete after day 24. CP-17,193-treated mice had not rejected the El4 allograft on day 24, while CYC-treated mice rejected the tumor allograft by day 17. CP-17,193 inhibited the formation of blasts sensitive to interleukin 2 (IL-2), had no effect on T cell proliferation using preformed blasts in the presence of added IL-2, and inhibited IL-2 production. Blast formation was significantly depressed at concentrations of CP-17,193 as low as 1.56 ug/ml. The immunosuppressive effects of CP-17,193 are explained by an inhibition of some initial step of lymphocyte activation which interferes with the T lymphocyte's ability to progress on to cell division and IL-2 production after stimulation. (33 Refs)

52. IMMUNOSUPPRESSIVE EFFECT OF ACUTE-PHASE REACTANT PROTEINS IN VITRO AND ITS RELEVANCE TO CANCER.

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Cancer Immunol Immunother; 13(1):38-43 1982

Several acute-phase reactant proteins (APRPs) were screened for their immunological effects to investigate immunosuppressive properties of serum from patients and animals with malignant disease. Concentrations used were determined by taking the highest levels observed in patients with metastatic cancer, then preparing one-half, one-quarter, and one-eighth dilutions. In the lowest concentration tested (1), none of the proteins significantly modified the response of normal lymphocytes to the phytohemagglutinin (PHA). At concentration 2, haptoglobin and fibrinogen significantly decreased lymphocyte response. At the lowest concentration tested (2) none of the proteins significantly inhibited monocyte chemotactic migration. At concentration 3 orosomucoid became inhibitory, while at the highest concentration (4), both haptoglobin and fibrinogen became inhibitory. Orosomucoid, alpha1-antitrypsin, and ceruloplasmin did not significantly depress the blastogenic response individually at any of the concentrations tested nor when they were combined in concentration 1. When combined in concentrations 2-4, significant suppression of the blastogenic response was observed. The blastogenic response was maximal with a PHA dilution of 1/32. Preincubation of cells with a 1/32 dilution of PHA for 2 hr, followed by washing and postincubation for 46 hr with phosphate-buffered saline produced a significant blastogenic response. When the post-incubation was performed with fibrinogen (concentrations 3 and 4) significant suppression was observed. (22 Refs)

53. COMPARATIVE GROWTH OF HUMAN TUMORS IN PHARMACOLOGICALLY IMMUNOSUPPRESSED, IMMUNE-DEPRIVED, CYCLOSPORIN A-TREATED AND NUDE MICE.

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Eur J Cancer Clin Oncol; 18(6):589-594 1982

The growth of three human tumor xenografts, namely on Ewing sarcoma, a colon carcinoma and an osteosarcoma, was compared in nude and conditioned mice. Conditioning protocols included (1) immune deprivation (thymectomy, lethal irradiation and cytosine arabinoside pretreatment); (2) immunosuppression with procarbazine, cyclophosphamide and antithymocyte serum; and (3) continuous administration of cyclosporin A. Similar tumor growth was seen in nude mice, immune-deprived mice and mice treated with the medium and high-dose immunosuppressive protocol. Cyclosporin A allowed only very modest tumor growth. In the main comparative experiment with the Ewing sarcoma and the colon carcinoma, overall survival was lowest with nude mice (17%), higher with immune-deprived mice (61%) and best with immunosuppressed mice (81 and 87%). For the screening of anticancer agents the immunosuppressive protocol consisting of synergistic procarbazine, cyclophosphamide and antithymocyte serum may be added to the already available models. It allows adequate tumor growth with good animal survival and does not require operative procedures and irradiation. (Author abstract) (16 Refs)

OTHER RELATED STUDIES

54. CHARACTERIZATION OF THE RECEPTORS FOR IGE ON MEMBRANES ISOLATED FROM RAT BASOPHILIC LEUKEMIA CELLS.

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Mol Immunol; 19(7):925-941 1982

Mast cells, basophils and a tumor analog, rat basophilic leukemia cells, have a surface receptor for immunoglobulin E (IgE). Membranes from such cells should be highly useful for the study of how the alpha- and beta-subunits of the receptor interact with the plasma membrane and function therein. Membranes were prepared from rat basophilic leukemia cells. The cells were reacted with radioiodinated IgE to saturate a fraction of their receptors and the radiolabel was used as a surface marker. When isolated from sucrose gradients, 40 +-10% yields of plasma membranes were obtained and these were typically purified 13-fold with regard to cellular proteins. Unoccupied receptors for IgE were almost all recovered (as assessed on membranes solubilized with detergent) as were surface-labeled proteins in general. The membrane-bound IgE appeared fully exposed as assessed with anti-IgE antibodies but surprisingly 70-80% of the unoccupied receptors present were unable to bind IgE when unsolubilized vesicles were tested. By electron microscopy the preparations appeared free of recognizable intracellular organelles. Though some of the membranes appeared multivesicular many showed large breaks in continuity. Assessment of permeability, carried out on dextran gradients, indicated that a significant number (greater than or equal to 50%) of the IgE-carrying membranes are not sealed. It is therefore most likely that both external and cytoplasmic aspects of the plasma membrane were exposed in many of the vesicles. Treatment of such membrane vesicles with trypsin or papain did not alter the apparent mol wt of the alpha-chain of the receptor or its binding activity for IgE. Additionally, when the vesicles were examined by enzyme-catalyzed iodination, no labeling of the receptor was observed under conditions where it is not labeled on intact cells (ie in the presence of IgE). These results suggest that either the alpha-chain of the receptor does not penetrate the membrane or that it cannot be modified by the particular probes we used. (Author abstract) (34 Refs)

55. A NEW MARKER FOR HUMAN CANCER CELLS. 1. THE CA ANTIGEN AND THE CA1 ANTIBODY.

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Lancet; 2(8288):1-6 1982

In a search for antibodies that might distinguish between malignant and non-malignant cells a panel of matched pairs of hybrid cells produced by fusion of diploid fibroblasts with malignant cells originating from a cervical carcinoma was used as a screen. Each pair consisted of a hybrid in which malignancy was suppressed and a malignant segregant derived from this hybrid. A monoclonal antibody, designated Ca1, was found that discriminated absolutely between the hybrids in which malignancy was suppressed and the malignant segregants. This antibody detected an antigen present in the cell membranes of a wide variety of malignant human cell lines but not of diploid human cell strains. The antigen was found in very low concentrations, if at all, in homogenates of normal adult or fetal tissues. It could be immunoprecipitated by the Ca1 antibody from extracts of malignant cells but not from extracts of non-malignant cells. After reduction, the immunoprecipitated antigen separated in sodium dodecyl sulfate acrylamide gels as two bands with approx molecular masses of 390,000 and 350,000. These two components had the properties of glycoproteins with a high carbohydrate content; both bound the Ca1 antibody. The antigenic determinant resisted boiling at 100 C and extraction by a range of organic solvents. The binding of the Ca1 antibody to the antigen was substantially reduced by treatment of the antigen with neuraminidase, and the antigenic determinant was largely destroyed by certain endoglycosidases and by extensive proteolysis. Pending its further characterization, this antigen has been called the Ca antigen. (Author abstract) (24 Refs)

56. PRODUCTION OF HEPATITIS B E ANTIBODY IN EPSTEIN-BARR VIRUS-INDUCED B LYMPHOCYTE CELL LINES.

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Kanagawa Prefectural Public Health Lab., 52-2 Nakao-cho, Asahi-ku, Yokohama 241, Japan
J Med Virol; 9(4):293-297 1982

A specific antibody-producing lymphocyte cell line (LCL) was established from peripheral blood lymphocytes of a donor carrying hepatitis B e (HBe) antibody (anti-HBe). Cultures were depleted of T-cells by removal of erythrocyte-rosetting cells, and were subsequently infected in vitro with Epstein-Barr virus. Upon initial establishment of the LCL anti-HBe could not be detected by solid-phase radioimmunoassay (RIA), double immunodiffusion, or reverse passive hemagglutination inhibition (R-PHI). However, after centrifugal harvesting of cells rosetting with HBe antigen-coupled sheep red blood cells the 10-fold concentrated supernatant showed the presence of anti-HBe by all three methods after 1 wk. The anti-HBe titer was 64-fold at 1 wk, 256-fold at 2 wk, 128-fold at 3 wk, but undetectable at 5 wk using R-PHI. RIA could not detect anti-HBe after 5 wk either. Anti-HBe activity in the culture supernatant was not destroyed by treatment with 0.2 M 2-mercaptoethanol at 2 wk, indicating that the antibody was not sensitive to this agent. and that the anti-HBe was IgG. The decline in anti-HBe activity in long-term cultures was not associated with any change in growth pattern. (12 Refs)

57. MONOCLONAL ANTIBODIES AND T-CELL HYBRIDOMAS. PERSPECTIVES AND TECHNICAL ADVANCES.

Hammerling GJ, Hammerling U, Kearney JF
Institut fur Immunologie und Genetik, Deutsches Krebsvorschungszentrum, Im Neuenheimer Feld 280, D-6900 Heidelberg, W. Germany
Monoclonal Antibodies and T-Cell Hybridomas. Perspectives and Technical Advances. Amsterdam, Elsevier/North-Holland Biomedical Press, Research Monographs in Immunology, Vol. 3, 587 pp., 1981.

Production of monoclonal antibodies to a wide range of antigens including antigens of the major histocompatibility complex of man and rodents, as well as other tissue antigens is presented. Reagents to detect and react with antigens from human tumors are described. Monoclonal antibodies to tissues other than those involved in neoplastic transformation are discussed. The use of monoclonal antibodies in the diagnosis of infectious diseases, particularly parasitic disease, is presented as are monoclonal antibodies to allergens and hormones. The use of monoclonal antibodies in analyzing immunological phenomena themselves, particularly aspects of idiotypic expression and interactions is discussed. The production of monoclonal antibodies by human hybridomas is described. T-cell hybridomas are a major advance in research of T-cell function and make T-cell products, both helper and suppressor factors, available for study. A practical guide for the derivation of antigen-specific hybridoma lines is provided. Human tumor-associated antigens are discussed with respect to those associated with solid tumors and melanomas, soluble products of tumors, and antibody-mediated tumor therapy. (1236 Refs)

58. TRANSPLANTATION OF LEUKEMIC BONE MARROW TREATED WITH CYTOTOXIC ANTILEUKEMIC ANTIBODIES AND COMPLEMENT.

Trigg ME, Poplack DG
Dept. Pediatrics, Univ. Wisconsin, Madison, WI, 53792
Science; 217(4556):259-261 1982

The ability of antiserum against murine L1210 leukemia to remove residual leukemia cells from murine bone marrow was investigated. Leukemic marrow was treated in vitro with antiserum and complement and used to hematologically reconstitute mice that had been irradiated with doses lethal to bone marrow. Following infusion of treated leukemic marrow, normal marrow returned without evidence of leukemia. More than 90 percent of the animals have survived for 11 mo without untoward effects, suggesting that the technique may be of use in the treatment of acute leukemia in humans. (Author abstract) (34 Refs)

59. AN IMPROVED METHOD FOR COVALENT ATTACHMENT OF ANTIBODY TO LIPOSOMES.

Shen DF, Huang A, Huang L
(c/o L. Huang) Dept. Biochemistry, Univ. Tennessee, Knoxville, TN, 37916
Biochim Biophys Acta; 689(1):31-37 1982

A rapid and simple method is described for the incorporation of monoclonal antibody coupled with palmitic acid into liposomes prepared by the reverse-phase evaporation method. Palmitoyl antibody in 0.15% deoxycholate is added to a liposome suspension after the majority of the organic solvent has been removed by evaporation. Efficient incorporation (over 80%) of palmitoyl antibody occurred without leakage of the encapsulated drug. Native, unmodified antibody did not incorporate under identical conditions. About 50% of the incorporated antibodies could be readily digested by protease, while most of an internal protein marker was not, suggesting that about half of the antibodies were exposed on the outer surfaces of liposomes. Target-specific binding of antibody-liposomes has also been demonstrated in vitro with the RDM-4 lymphoma cells. This method offers a rapid and highly efficient attachment of functional antibody molecules to liposomes with high capture efficiency of drugs, and therefore should be useful in target-specific delivery of drugs mediated by liposomes. (Author abstract) (15 Refs)

60. PLATINUM-COMPLEXED ANTITUMOR IMMUNOGLOBULINS THAT SPECIFICALLY INHIBIT DNA SYNTHESIS OF MOUSE TUMOR CELLS.

Hurwitz E, Kashi R, Wilchek M
Dept. Biophysics, Weizmann Inst. Science, Rehovot 76100, Israel
JNCI; 69(1):47-51 1982

Platinum salts were complexed with antitumor reactive immunoglobulins (Ig). The Pt-complexed antitumor Ig retained their specific antibody binding activity. The inhibition of DNA synthesis by Pt salts ($K_2 PtCl_4$ and cis-diamminedichloroplatinum II) and Pt-Ig complexes was studied in two tumor cell lines of mice. The Pt-Ig complexes were much more effective inhibitors of DNA synthesis when complexed with Ig, which had binding affinity toward the test tumor cells. (Author abstract) (27 Refs)

61. AUTOLOGOUS BONE-MARROW TRANSPLANTATION IN CALLA-POSITIVE ACUTE LYMPHOBLASTIC LEUKAEMIA AFTER IN-VITRO TREATMENT WITH J5 MONOCLONAL ANTIBODY AND COMPLEMENT.

Ritz J, Bast RC, Clavell LA, Hercend T, Sallan SE, Lipton JM, Feeney M, Nathan DG, Schlossman SF
Div. Tumor Immunology, Sidney Farber Cancer Inst., 44 Binney St., Boston, MA, 02115
Lancet; 2(8289):60-63 1982

A monoclonal antibody (J5) specific for the common acute-lymphoblastic-leukemia antigen (CALLA) was used for in-vitro pre-treatment of bone-marrow before autologous transplantation in four patients with CALLA positive acute lymphoblastic leukemia (ALL) in relapse, who did not have HLA-compatible donors. After remission induction and intensification, bone-marrow cells were harvested, treated with J5 antibody and rabbit complement, and cryopreserved in liquid nitrogen. Patients received ablative chemotherapy and total-body irradiation before reinfusion of autologous J5-treated bone marrow. The transplantation protocol was well tolerated, and engraftment of normal myeloid cells occurred in all four patients. Two patients have continued in unmaintained remission with complete hematopoietic reconstruction for more that 1 yr after autologous transplantation. (Author abstract) (23 Refs)

62. DEPRESSED CELL MEDIATED IMMUNITY AND HYPERIMMUNOGLOBULINAEMIA IN PATIENTS WITH LYMPHOMAS.

Tuteja N, Kapoor AK, Rathi AK, Mehrotra RM, Kumar A, Kushwaha MR
Clinical Immunopathology Unit, Dept. Pathology, K. G. Medical Coll., Lucknow, India
J Indian Med Assoc; 78(4):63-66 1982

The significant finding of the present study was the detection of impaired CMI and hyperimmunoglobulinemia in majority of the patients with lymphomas. Defects in CMI were evident even during early stages of the disease. It appeared that there is a definite need to boost up T-cell mediated responses and to control the overactivity of B-cell in these patients. Proper handling of the immune system by appropriate therapy might change the course of this disease. (Author abstract) (16 Refs)

63. EFFECT OF T AND B CELL IMMUNOSUPPRESSION ON THE RELEASE OF MAREK'S DISEASE VIRUS FROM THE FEATHER FOLLICLES OF CHICKENS.

Gupta SK, Kharole MU, Kalra DS
Dept. Veterinary Pathology, Haryana Agricultural Univ., Hissar 125 004, India
Indian J Exp Biol; 20(2):179-180 1982

The release of Marek's disease virus (MDV) from feather follicles of Marek's disease infected chicks was delayed by 2 wk in chicks vaccinated with herpes virus of turkeys (HVT). T cell suppression (by thymus ablation and antithymus treatment) and B cell suppression (by injection of cyclophosphamide and anti-bursa serum treatment) had no significant effect on release of MDV in HVT vaccinated chickens. (12 Refs)

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